ORIGINAL ARTICLE

Managing Congestive Heart Failure in a General Hospital in Malaysia. Are We Keeping Pace With Evidence?

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Summary

Evidence-based heart failure management now includes beta-blockers and spironolactone in addition to diuretics and angiotensin-converting enzyme inhibitors. We aim to determine if these recommendations had been applied in practice for acute and chronic stable heart failure, and what difficulties there might be. Data from 80 consecutive patients hospitalized for decompensated heart failure ('acute') between May and July 2003 were analyzed at admission, upon discharge and at 12 weeks follow-up; along with 74 cardiology clinic out-patients with stable congestive heart failure ('chronic'- no decompensation or admission in previous six months). Less than half of study patients with prior left ventricular dysfunction were on ACE-inhibitors (47%), diuretics (39%), ATII antagonists, spironolactone or digoxin (5% each). All 'acute' patients were commenced on diuretics and ACE-inhibitors in hospital. Six patients died or transferred to another center. Compliance with clinic appointment at 12 weeks was 85% despite telephone reminders. Drug prescription at 12 weeks was significantly lower for diuretics and ACE-inhibitors compared to prescription at discharge (all $p<0.05$) but higher compared to patients with chronic HF. Diuretics and ACE inhibitors remain under-utilized for patients with recurrent heart failure. Use of spironolactone and beta-blocker is slow due to limited medical experience and funding. Clinic non-attendance is significant and due to patient factors.

Key Words: Heart failure, Evidence-based medicine, Medical therapy, Compliance

Introduction

Congestive heart failure (CHF) is a clinical presentation characterized commonly by dyspnoea, pulmonary and peripheral oedema, supported by echocardiographic or other investigative findings of ventricular dysfunction [1]. For patients with severe left ventricular dysfunction, the mortality rate is thought to exceed 50% over a year without medical intervention [2]. The landmark CONSENSUS trial and subsequent trials in the last quarter of century have provided fresh optimism for the clinician, who can now prescribe -in addition to a diuretic- an angiotensin converting enzyme inhibitor (ACE-I) [2,3], an aldosterone antagonist [4], and a beta-blocker [5,6] at various stages or severity of heart failure, including asymptomatic left ventricular dysfunction [3]. Indeed, each of these classes of drugs had been shown to reduce mortality by 20 to 50% in the large multi-center clinical trials. Applying any recommendations from clinical trials to clinical practice is not always easy even for established treatment regimes such as aspirin use in ischemic heart disease [7] and anticoagulation for atrial fibrillation [8]. Guidelines for heart failure management have been generally better-received and adopted in hospitals of developed countries [9].

This article was accepted: 13 January 2006

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Our hospital is a large general hospital with over 600 acute beds in the capital of the largest state in West Malaysia and serves a general population of over one million – largely rural - residents. Its budget, setup and population covered are similar to other general hospitals in the country. As a secondary referral center with a dedicated cardiology unit and clinic, we expect to comply with, and set the example for the management of acute and chronic compensated heart failure [10]. Whether this is being done is not known. Our aim therefore is to determine if patients admitted with acute decompensated heart failure had been optimally treated prior to hospitalization, and subsequently discharged and followed up in the clinic with appropriate treatment according to evidenced-based medicine.

Materials and Methods

We recruited eighty consecutive patients hospitalized for decompensated heart failure (termed as 'acute') between May and July 2003. The initial diagnosis was verified by the attending doctor with at least two years clinical experience. Patients were classified in their severity of clinical heart failure according to the New York Heart Association (NYHA) score –class I and II being mild, class III and IV being severe. All patients were seen by a medical specialist within 48 hours of admission. Trans-thoracic echocardiography was performed by a single trained operator using ALOKA ® on the ward or in the cardiology department. Venous blood was collected and sent to the pathology laboratory for haemoglobin concentration (gram/litre). A history of hypertension is defined as systolic blood pressure equal to or greater than 160mmHg and/or diastolic blood pressure equals to or greater than 90mmHg, or being on treatment for hypertension. Ischemic heart disease is defined by previous documented myocardial infarction, angina pectoris, positive exercise stress test or angiographically-proven coronary disease. Valvular heart disease is defined as documented moderate to severe mitral or aortic stenosis or incompetence. Atrial fibrillation is noted if it were documented at any time over the last two years. Patients with moderate to severe renal impairment (serum creatinine greater than 220microM/l), liver impairment (serum aspartate transaminase greater than 45 U/L), acute infective and inflammatory illnesses, thyrotoxicosis, Conn's syndrome, phaeochromocytoma, and malignancy were excluded. Patients with diabetes mellitus with hypertension or albuminuria were excluded as they represented a select group of patients who require angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin II receptor antagonists (ATIIA) [11,12]. Conversely, ACE-inhibitors are relatively contraindicated in patients with moderate to severe aortic stenosis and hypertrophic obstructive cardiomyopathy therefore these patients were also excluded.

Therapies on admission and upon discharge were recorded. All patients discharged from the hospital were offered an out-patient clinic appointment at 6 and 12 weeks, with data collection performed at 12 weeks follow-up. A second group of seventy-four patients attending out-patient cardiology clinics for heart failure but had been stable without decompensation, deterioration in NYHA class or hospitalization in the prior six months (termed 'chronic') were also recruited. The same exclusion criteria applied.

All patients were informed of their participation in a data collection study not involving additional blood tests or invasive procedures and consent was obtained. The study has the approval of the local research ethics committee and the medical advisory committee.

Statistical analysis

Patient age, left ventricular ejection fraction (LVEF), systolic and diastolic blood pressures (SBP and DBP respectively) and serum haemoglobin (Hb) are parametric and expressed as Mean ± 1standard deviation (s.d.). Inter-group comparisons were conducted using 2-sample T-tests. Other parameters are expressed as absolute numbers with percentages expressed in brackets, and compared using Chi-Square. A P value of less than 0.05 is considered statistically significant. Data were collected and analyzed using Microsoft Excel 2000.

Results

Cohort

Acute heart failure patients comprised 10% of all adult acute medical admissions during a three month period between May and July 2003. All 'acute' patients had NYHA III or IV while all but four of the patients in the 'chronic' group were in NYHA I-II. Acute heart failure patients were older, with higher blood pressures but lower LVEF (see Table I). Ischemic heart disease was more frequent in the 'acute' group but valvular disease less so. Heart failure or left ventricular dysfunction was also documented in 45% of 'acute' patients but only 18% were under any active medical follow-up.

We divided the eighty 'acute' group into patients with prior documented heart failure of left ventricular dysfunction (termed 'recurrent', N=38), and those without (presenting therefore with 'new' heart failure, N=42). Among new heart failure patients, men outnumbered women two-to-one. This group also had higher rates of ischemic heart disease but less valvular heart disease and dilated cardiomyopathy.

Baseline drug therapy
Patients with 'recurrent' heart failure showed significantly higher rates of use of diuretics, ACE-inhibitors, ATII antagonists, spironolactone and digoxin compared to those with 'new' heart failure although use in all were less than 50% (see Table II). Patients with acute heart failure (new or recurrent) showed significantly lower rates of use of diuretics, ACE-inhibitors, spironolactone and digoxin compared to chronic heart failure patients.

Frusemide was the diuretic of choice in all patients. Two patients in the 'acute' group were on low dose hydrochlorothiazide in combination with losartan (Hyzaar ®) in addition to frusemide. For ACE-I and ATIIA, captopril was the most commonly used but prescribed at less than the usual recommended maintenance dose (data not shown). Perindopril and losartan were the other drugs in these classes respectively. For beta-blockers, short-acting metoprolol was widely used while carvedilol was used only in 'chronic' out-patients. Carvedilol was commenced in all cases by a physician or cardiologist. Bisoprolol and long-acting metoprolol were not used. Aspirin was the anti-platelet agent of choice when indicated. Oral nitrate preparations were used but as part of anti-anginal therapy and not as a vasodilator treatment for heart failure. No patients were on concomitant hydralazine with nitrates for heart failure [13].

Admission and Discharge
From admission, all 'acute' patients were commenced on diuretics and ACE-inhibitors. The median length of stay was ten days [inter-quartile range 6-21]. Six patients died or transferred to another center. All remaining patients were offered an out-patient appointment at the cardiology or medical out-patient clinics at the time of discharge with the appointment clearly recorded and communicated to the patient by the ward nurse.

Prescriptions on discharge and at 12 weeks were compared (see Table III). Two patients had significant deterioration of serum creatinine of more than 30% from baseline and three developed intractable cough shortly after commencing ACE-inhibitors. All three patients who developed cough were started on an ATIIA. A further four patients refused to continue with ACE-inhibitors. Four patients were started on spironolactone and one was started on carvedilol.

Follow-up
At six weeks, sixty-one patients (82%) attended clinic. The other patients were contacted by phone and a new appointment made. Sixty-three patients attended at 12 weeks (15% drop-out). Five patients who had missed the first appointment attended the second, including two out of the three patients who had been re-admitted. Seven patients missed both appointments. Lack of transportation was the reason, if any, offered for not turning up. No deaths were documented although three patients were not contactable at 12 weeks.

Discussion

Heart failure is a common cause of acute adult medical admission in our hospital. This is due partly to increased survival from myocardial infarction and a generally ageing population [14,15]. We found that most of the patients admitted with acute heart failure were not under active medical follow-up despite a significant number of them having heart failure or left ventricular dysfunction. An important effect of not seeing these patients on a regular basis may be failure to optimize or start medical treatment that has been proven to reduce mortality [2-6]. In our study, less than half of the acute heart failure patients with previous left ventricular dysfunction were taking diuretics and ACE-inhibitors at the time of admission. Patients with underlying hypertension and ischemic heart disease may also have been overlooked at the primary or secondary prevention level leading to an excess of new acute heart failure cases stemming from untreated or inadequately-treated cardiac ischemia and hypertension [16].

There is a high clinic default rate immediately after discharge. We had presumed that an ineffective follow-up system where patients were either not offered an out-patient appointment, not appropriately referred to a specialist center or simply defaulted and failed to be offered a new appointment, to be an important reason for the large numbers of heart failure patients not being regularly followed-up. However, the reasons that have been cited by patients for failure to attend clinic after discharge were lack of transport, inconvenience or personal choice. Patients who failed to attend the first appointment were unlikely to return for subsequent

Table I: Comparison of baseline characteristics of patients admitted with acute decompensated heart failure (all 'acute') – including those with prior documented left ventricular dysfunction or heart failure ('acute' recurrent) and patients with first episodes of heart failure ('acute' new) - and patients attending out-patient clinic for stable, compensated left ventricular dysfunction ('chronic')

	All 'acute' HF (n=80)	'acute new' (n=42)	'acute recurrent' (n=38)	'chronic' HF (n=74)	P value (all acute versus chronic)
Age (years)	56 ± 7	49 ± 15	58 ± 7	42 ±18	0.04
Gender (Male:Female)	48:32	29 :13	19 : 19*	52 : 22	0.03
Malay vs. Non-Malay	55:25	29 :13	26 : 12	53 : 21	0.33
Ejection Fraction (%)	30 ± 3	30 ± 5	29 ± 5	35 ± 5	0.03
Systolic BP (mmHg)	160 ± 15	160 ± 8	120 ± 28**	120 ± 18	0.01
Diastolic BP (mmHg)	90 ± 9	100 ±12	85 ± 15	64 ± 7	<0.01
Haemoglobin (g/dL)	8.8 ± 1.3	12 ±1.5	8.2 ± 0.3**	10 ± 0.7	0.06
Hypertension (%)	34 (42)	20 (48)	18 (47)	29 (39)	0.34
IHD (%)	52 (65)	35 (83)	17 (45)**	37 (50)	<0.01
Valvular heart disease (%)	10 (13)	1 (2)	9 (24)**	18 (24)	<0.01
Dilated cardiomyopathy	4 (5)	0 (0)	4 (11)**	8 (11)	0.06
Atrial Fibrillation (%)	12 (15)	4 (11)	8 (21)*	16 (22)	0.10

HF, heart failure; IHD, ischemic heart disease; BP, blood pressure; ACE-I, angiotensin-converting enzyme inhibitors; ATIIA, angiotensin II receptor antagonist.
Parametric values expressed as Mean 1s.d. and analyzed using 2-sample t-test. Dichotomous variables expressed as absolute number and (percentages) and compared with Chi square. P value less than 0.05 is statistically significant.
* p value less than 0.05 and ** p value less than 0.01 when comparing the 'acute' recurrent HF sub-group versus 'acute' new HF sub-group.

Table II: Comparison of baseline drug therapy of acute heart failure patients with previous heart failure or known left ventricular dysfunction ('acute-recurrent' HF) and patients with first episode of failure ('acute-new' HF) and with chronic stable heart failure out-patients ('chronic' HF)

Medications on presentation	All 'acute' HF (n=80)	'acute new' HF (n=42)	'acute recurrent' HF (n=38)	'chronic' HF (n=74)	P value (acute new vs. recurrent HF)
Diuretics (%)	19 (24)**	4 (11)	15 (39)^	62 (84)	<0.001
ACE-I (%)	30 (37)**	12 (29)	18 (47)^	55 (74)	0.012
ATIIA (%)	2 (3)	0 (0)	2 (5)^	2 (3)	<0.001
Spironolactone (%)	2 (3)*	0 (0)	2 (5)^	7 (9)	<0.001
Beta-blocker (%)	32 (40)**	30 (71)	2 (5)^	11 (15)	<0.001
Digoxin (%)	6 (8)*	2 (5)	4 (11)^	13 (18)	0.09
Warfarin (%)	4 (5)*	4 (11)	0 (0)^	9 (12)	0.06
Anti-platelet agent (%)	57(71)**	37 (88)	20 (53)^	33 (45)	< 0.001

BP, blood pressure; ACE-I, angiotensin-converting enzyme inhibitors; ATIIA, angiotensin II receptor antagonist. Parametric values expressed as Mean 1s.d. and analyzed using 2-sample t-test. Dichotomous variables expressed as absolute number and (percentages) and compared with Chi square. P value less than 0.05 is statistically significant.
* p value less than 0.05 and ** p value less than 0.001 when comparing all' acute HF versus 'chronic' HF.
^ p value less than 0.001 when comparing acute recurrent HF sub-group with 'chronic' HF.

Table III: Comparison of drug prescription for acute heart failure patients at the time of admission, discharge and at 12 weeks follow-up and with chronic stable heart failure patients in the clinic.

	'acute' HF on admission (n=80)	'acute' HF on discharge (n=74)ø	'acute' HF at 12 weeks (n=63)ø	'chronic' HF (n=74) (n=74)	P value ('acute' HF on discharge vs. 12 weeks)
Diuretics (%)	19 (24)*	74 (100)	50 (94)	62 (84)	<0.001
ACE-inhibitors (%)	30 (37)*	70 (94)	52 (83)	55 (74)^	0.001
ATII Antagonist (%)	2 (3)	2 (3)	5 (8)	2 (3)^	0.02
All ACE-I and ATIIA (%)	32 (40)*	72 (97)	57 (90)	57 (77)^^	0.01
Spironolactone (%)	2 (3)	3 (4)	6 (10)	7 (9)	0.05
Beta-blockers (%)	32 (40)*	4 (5)	4 (6)	11 (15)^^	0.15

HF, heart failure; ACE-I, angiotensin-converting enzyme inhibitors; ATIIA, angiotensin II receptor antagonist; mg, milligrams. Values are discrete, expressed as absolute number and (percentages) and compared with Chi square. P value less than 0.05 is statistically significant.

* p value less than 0.01 comparing 'acute' HF on admission versus 'acute' HF on discharge.

^ p value less than 0.05 and ^^ p value less than 0.01 when comparing 'acute' HF at 12 weeks versus 'chronic' HF.

ø 6 patients died or transferred to another centre. 11 patients did not attend clinic at 12 weeks.

appointments even with reminders made. Hence it appears that the patient, rather than the system, is more to blame for the high clinic default rate. As patients in our hospital normally rely on hospital prescription and dispensing of medications, we assumed that these patients would become non-compliant after their medications run out.

Ward treatment of acute decompensated heart failure was in all circumstances appropriate. Diuretics were commenced and tailored to symptoms. ACE-inhibitors were changed to ATII antagonists when irritable cough supercede or stopped in the presence of deteriorating renal function. Beta-blockers were generally stopped in acute heart failure on admission and later recommenced at reduced doses or using the non-selective long-acting carvedilol. Both beta-blockers and spironolactone were recommended only after heart failure has stabilized [4,6].

At the clinic, we found about 6% of the acute patients attended had been non-compliant with their ACE-inhibitors. If the data from the chronic heart failure group were regarded as typical of patients having attended clinic for more than six months, then perhaps the large number of patients who were not on ACE-inhibitors in the chronic group (26%) may have been non-compliant by choice, rather than as a result of the physician's failure to initiate them. Is this also the case for half of the acute heart failure patients with known left ventricular dysfunction but were not on ACE-inhibitors? The real reason is most probably patient refusal as well as failure on the doctor's part to either initiate or explain the benefit of the drug to the patient. Yet, in our study, only one patient who had not been compliant following discharge was successfully persuaded to recommence the medications. The other three persisted to refuse them after discussing at length the merits of these drugs.

Other classes of drugs, carvedilol in particular, is clearly limited by experience, drug availabitlity and exposure to recent trials. One such trial is the COMET study [17] which clearly showed a benefit of carvedilol over short-acting metoprolol and therefore recommends against the current practice. Lack of experience and funds are also the commonest reasons for failing to optimize the dose of carvedilol.

Study Limitation

This study is limited by its small numbers in the 'acute' group preventing further analysis of patients who were followed-up in clinic compared to those without active medical follow-up. It was also not possible to trace the discharge histories of many of the 'chronic' stable heart failure patients who were attending out-patients, thus we were unable to determine the actual non-compliance rate of medications that had been started prior to discharge.

Conclusion

In conclusion, heart failure is a common cause of medical admission. Untreated or inadequately-treated cardiac ischemia and hypertension are the main causes of new failure cases while lack of regular monitoring may contribute to recurrent failure. Non-attendance at clinic and non-compliance with drugs are largely due to patient choice while adoption of latest evidence such as use of spironolactone and beta-blocker is slow and due to limited physician experience and funding.

Acknowledgements

This study has been facilitated by the Kuantan Research Centre, Hospital Tengku Ampuan Afzan, Kuantan, Pahang. We are grateful for the staff on the medical wards and medical out-patients department for their help in tracing the medical records.

Addendum

Since the completion and submission on this article, Bisoprolol (a third generation selective beta-blocker) has been made available for prescription in the medical out-patient department for heart failure treatment by physicians.

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