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Adherence to treatment guidelines in the pharmacological management of chronic heart failure in an Australian population

Dao-Kuo Yao[1, 2], Le-Xin Wang[2], Shane Curran[2,3], Patrick Ball[2]

[1] *Department of Cardiology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China*

[2] *School of Biomedical Sciences and Centre for Inland Health, Charles Sturt University, Wagga Wagga, NSW 2678, Australia*

[3] *Department of Emergency Medicine, Wagga Wagga Base Hospital and Rural Clinical School, University of New South Wales, Wagga Wagga, NSW 2650, Australia*

Abstract

Background To document the pharmacotherapy of chronic heart failure (CHF) and to evaluate the adherence to treatment guidelines in Australian population. **Methods** The pharmacological management of 677 patients (female 46.7%, 75.5 ± 11.6 years) with CHF was retrospectively analyzed. **Results** The use of angiotensin converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARB) and β-blockers were 58.2 % and 34.7 %, respectively. Major reasons for non-use of ACE inhibitors/ARBs were hyperkalemia and elevated serum creatinine level. For patients who did not receive β-blockers, asthma and chronic obstructive pulmonary disease were the main contraindications. Treatment at or above target dosages for ACE inhibitors/ARBs and β-blockers was low for each medication (40.3% and 28.9%, respectively). **Conclusions** Evidenced-based medical therapies for heart failure were under used in a rural patient population. Further studies are required to develop processes to improve the optimal use of heart failure medications.

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Keywords: heart failure; ACE inhibitors; angiotensin receptor; β-blockers; prognosis

1 Introduction

Chronic heart failure (CHF) has emerged as a major public health problem in Australia. Improved survival after myocardial infarction combined with an aging population, means a heart failure epidemic may appear within the next two decades.[1–3] Despite considerable advances in treatment to increase long-term survival, CHF is still associated with a high mortality rate.[4]

Pharmacotherapy is an important component of CHF management which not only improves symptoms but also reduces cardiac remodeling and neuro-endocrine activation to prevent worsening of symptoms and reduces mortality.[5] Accumulated evidence shows that ACE inhibitors/Angiotensin II receptor blockers (ARBs) and β-blockers could reduce the high mortality in patients with CHF.[6,7] Furthermore, better implementation of pharmacotherapy was associated with better prognosis in patients with CHF.[8,9]

In prior studies of Australian population, ACE inhibitors/ARBs and β-blockers were underutilized in some medical centres, especially in rural regions where the prevalence of heart failure is higher than capital city and metropolitan areas.[10-12] However, a recent study in Western Australia showed ACE inhibitors/ARBs and β-blockers use was more evidenced based.[13]

Little is known about current heart failure management regimes in other rural regions of Australia, which may differ from those reported a decade ago. The aim of the present study was to investigate the status of pharmacotherapy, especially the use of ACE inhibitors/ARBs and β-blockers, in CHF patients in a regional medical centre, and to compare with the present CHF management guidelines.

2 Methods

This study is a retrospective analysis of medication use for in-patient management of CHF in Wagga Wagga Base Hospital, a major regional hospital in rural New South Wales. From Jan 2003 to Dec 2007, medical records of 667 consecutive in-patients with heart failure were selected and reviewed by the investigators. Entry criteria for the study required a diagnosis of CHF according to the 2006 Australian guidelines, *i.e.,* on the basis of the presence of typical

Correspondence to: Le-Xin Wang, PhD, Cardiovascular Research Group, Charles Sturt University, Wagga Wagga, NSW 2678, Australia. Email: lwang@csu.edu.au

Telephone: +61-2-69332905 **Fax:** +61-2-69332587

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clinical features and appropriate investigation.[5] This study received approval from the Ethics Committees for Human Research of the Charles Sturt University and the Greater Southern Area Health Service.

Baseline clinical data, prescription patterns and use of medical resources were recorded in all patients. When multiple etiological factors for heart failure were present, the one judged by the cardiologists to be predominant was identified as the primary cause. Electrocardiography, serum creatinine level and serum potassium level were measured in hospital for all patients.

All prescribed medications and dosing schedules were recorded. Dosing adequacy of ACE inhibitors/ARBs and β-blockers was gauged against recommendations from guidelines for CHF treatment of Australia (2006). Target doses achieved of ACE inhibitors/ARBs and β-blockers were recorded according to the ESC guidelines (2008).[14] For patients not prescribed ACE inhibitors/ARBs, contraindications including chronic renal failure (serum creatinine > 220 μmol/L), hyperkalemia (serum potassium > 5.0 mmol/L), bilateral renal artery stenosis, severe aortic stenosis and angioedema were noted. For patients not prescribed β-blockers, contraindications included asthma, second or third degree heart block, sick sinus syndrome (in the absence of a permanent pacemaker) and sinus bradycardia (< 50/min).[14]

2.1 Statistical analysis

Data are summarized as mean ± SD. The characteristics of patients' medication use were summarized with descriptive statistics. A P value of less than 0.05 was considered statistically significant. All analyses were performed using SPSS 13.0 (SPSS Inc, USA).

3 Results

The clinical and demographic characteristics of the studied population are presented in Table 1. Over 50% of patients were class 3–4 by NYHA classification of heart failure. Ischaemic heart disease was the most common cause of heart failure, affecting 55.5% of patients, although hypertension was documented in 62.5% of patients. Common co-morbidities were hypertension, myocardial infarction (MI), arrhythmia, hypercholesterolemia, chronic obstructive pulmonary disease (COPD) and arthritis. In patients with arrhythmia (31.8%), the most common type was atrial fibrillation. Left ventricular ejection fraction (EF) was assessed by echocardiography in 242 (36%) patients. Among these, preserved systolic function, defined as a left ventricular EF of 45% or greater, was identified in 50.4%.

Table 1. Clinical characteristics of patients with heart failure (n = 677). Values are mean ± SD or n (%).

Variables	Data
Age (years)	75.5 ± 11.6
Female	316 (46.7)
Duration in hospital (days)	5.7 ± 8.3
Number of past hospitalisations	7.5 ± 8.1
NYHA class III-IV	347 (51.3)
Etiology	
Ischaemic	376 (55.5)
Non-ischaemic	301 (44.5)
Co-morbidities	
Hypertension	423 (62.5)
Angina	97 (14.3)
MI	249 (36.8)
CABG	132 (19.5)
Cardiomyopathy	64 (9.5)
Valvular	75 (11.1)
Arrhythmia	215 (31.8)
Pacemaker	81 (12)
Diabetes	193 (28.5)
Hypercholesterolemia	145 (21.4)
Stroke	78 (11.5)
Depression	62 (9.2)
COPD	199 (29.4)
Arthritis	133 (19.6)
Systolic BP < 100 mmHg	39 (5.8)
Heart rate ≥ 100/min	203 (30.0)
ECG assessment	
Atrial fibrillation/flutter	156 (23.0)
Sinus tachycardia	67 (9.9)
Ventricular tachycardia	4 (0.6)
LV function assessment	242 (35.7)
EF ≥ 45%	122 (50.4)
EF < 45%	120 (49.6)
Serum potassium > 5.0 mmol/L	141 (20.8)
Serum creatinine > 220 μmol/L	79 (11.7)
Serum potassium > 5.0 mmol/L and creatinine > 220 μmol/L	38 (5.6)

NYHA: New York Heart Association; MI: myocardial infarction; CABG, coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; BP: blood pressure; ECG: electrocardiography; LV: left ventricle; EF: ejection fraction.

As shown in Table 2, ACE inhibitors or ARBs were used in 394 (58.2%) patients, with ACE inhibitors in 296 (43.7%) and ARBs in 121 (17.9%). Twenty-three patients simultaneously

Table 2. Cardiovascular medication use in patients with chronic heart failure.

Agents	*n* (%)
ACE inhibitors or ARBs	394 (58.2)
ACE inhibitors	296 (43.7)
ARBs	121 (17.9)
ACE inhibitors + ARBs	23 (3.3)
β-blockers	235 (34.7)
ACE inhibitors +*β*-blockers	130 (19.2)
Diuretics	488 (72.0)
Digoxin	126 (18.6)
Spironolactone	78 (11.5)
CCBs	74 (10.9)
DHPs	46 (6.8)
Non-DHPs	28 (4.1)
Statins	148 (21.9)
Aspirin	257 (38.0)
Clopidogrel	35 (5.2)
Warfarin	141 (20.8)
Amidarone	34 (5.0)
Sotalol	10 (1.5)
Nirates	94 (13.9)

ACE: angiotensin converting enzyme; ARBs: angiotensin receptor blockers; CCB: calcium channel blocker; DHPs: dihydropyridines.

Table 3. Non-usage and possible reasons of ACE inhibitors and *β*-blockers.

Agents non-used	*n*	Possible reasons	*n* (%)
ACE inhibitors/ ARBs	283	Serum potassium > 5.0 mmol /L	141 (49.8)
		Serum creatinine > 220 μmol/L	79 (27.9)
		Systolic BP < 80 mmHg	0 (0.0)
		Unknown	101 (35.7)
β-blockers	442	Asthma	44 (9.9)
		Complete atrioventricular block	1 (0.0)
		Systolic BP < 80 mmHg	0 (0.0)
		HR < 50 /min	5 (1.1)
		COPD	155 (35.0)
		Unknown	237 (53.6)

Table 4. Target doses achieved of ACE inhibitors/ARBs and *β*-blockers.

Agents	Target doses achieved *n*(%)
ACE inhibitors / ARBs	159 (40.3)
β-blockers	68 (28.9)

received ACE inhibitors and ARBs. *β*-blockers were used in 235 (34.7%) patients in this group. Other common cardiovascular drugs include diuretics (72%), digoxin (18.6%), spironolactone (11.5%), aspirin (38.0%), warfarin (20.8%), statins (21.9%), and nitrates (13.9%).

As shown in Table 3, among patients not receiving ACE inhibitors (n = 283), contraindications were documented in 64.3% (n = 182), including 141 (49.8%) with repeated reading serum potassium > 5.0 mmol/L, 79 (27.9%) with repeated reading serum creatinine > 220 μmol/L (38 cases had both serum potassium > 5.0 mmol/L and serum creatinine > 220 μmol/L). In another 101 patients, no definite contraindications were identified. Among patients not receiving *β*-blockers, contraindications were documented in 50 patients, including 44 (9.9%) with asthma, five cases with heart rate < 50 beats/minutes at admission, and one case with complete heart block. Other possible reasons for not receiving *β*-blockers may be concomitant COPD, which was present in 155 patients (Table3).

Target-dosages of ACE inhibitors/ARBs were achieved in 159 patients, which accounted for 40.3% of patients who received ACE inhibitors/ARBs. Target-dosages of *β*-blockers were achieved in 68 patients, which accounted for 28.9% of patients who received *β*-blockers (Table 4).

4 Discussion

In this study, we have shown that ACE inhibitors/ARBs and *β*-blockers were underused in patients with heart failure in a rural Australian hospital, compared with published guidelines. Main reasons of non-use of these drugs were elevated serum potassium and creatinine level for ACE inhibitors/ARBs, and asthma for *β*-blockers. The proportion of patients who achieved target-dosage of ACE inhibitors/ ARBs and *β*-blockers was also low.

In the analysis of Cardiac Awareness Survey and Evaluation (CASE) study[2,10], which was conducted in Australia in 1998, the prescribing rate of ACE inhibitors and *β*-blockers were 51.4% and 12.6% respectively in rural towns. The ACE inhibitors usage in our study was lower than that in the CASE study; however, the use of *β*-blockers, and ACE inhibitors along with *β*-blockers was higher than that of the CASE study. The higher use of *β*-blockers and ACE inhibitors combined with *β*-blockers compared to the CASE study may reflect increased evidenced based therapy over the study period.

The major reason relating to low usage of ACE inhibitors in our study is perceived contraindications. We noted that 26% of the patients had hyperkalemia or serum creatinine levels of 220 μmol/L or higher, thus restricting the use of

ACE inhibitors or ARBs if these were true and repeated findings. However, 35.6% of the patients who did not receive ACE inhibitors/ARBs had no identifiable contraindications. One possible explanation is that some physicians may have concerns over polypharmacy and the risk of side effects in elderly heart failure patients (average 75.5 years in our cohort). In patients > 65 years, β-blockers, ACE inhibitors and ARBs have similar mortality benefit to that observed in younger patients.[15] Therefore, these agents should be prescribed to all elderly patients in the absence of contraindications. Another potential barrier for underuse is at the patient level, as age, disease severity, comorbidities and concomitant drug intake may impact on the prescriptions of heart failure medications.[16]

For β-blockers, the most common reasons for underprescribing may be concerns about the possible side effects, co-morbidities, polypharmacy, or contraindications such as asthma. However, in our patients who did not receive β-blockers, few had a genuine contraindication. These results are in line with the recent Euroheart survey.[17] Co-morbidities and other therapies had a significant impact on the use of β-blockers, which were more often prescribed to patients with ischaemic heart disease and less often to patients with COPD. In this study, 35% of the patients who did not receive β-blockers had COPD, which is not considered as a compelling contraindication for β-blockers. Severity of heart failure symptoms may also affect the use of β-blockers. In patients with volume overload or recent treatment with positive inotropic agents, therapy with β-blockers may be delayed, although these patients may tolerate therapy well during initiation and upward dose titration.[18]

In our study, 23 patients received ACE inhibitors additional to ARBs. This may be due to severe heart failure and patients remaining symptomatic despite optimal treatment with an ACE inhibitor and β-blockers, as indicated in ESC guideline 2008.[15] However, addition of ARBs in patients already receiving treatment of ACE inhibitors and β-blockers may be associated with a worse outcome and more side effects.[19,20] Therefore, in most conditions, ARBs should only be used as an alternative for patients unable to tolerate ACE inhibitors.

Target dosages were achieved in 40.3% of patients on ACE inhibitors/ARBs and in 28.9% on β-blockers, which were consistent with results of a recent study,[21] but lower than the recommended high target doses.[14] Large-scale trials showed that target doses of ACE inhibitors/ARBs and β-blockers provide the optimal improvement in left ventricular function and reduction in mortality and hospitalizations.

In summary, in this retrospective study, ACE inhibitors/ARBs and β-blockers were underprescribed in patients with CHF. Target doses achieved for both drug groups were also lower than the international standards. Contraindications to ACE inhibitors/ARBs and β-blockers were the major reasons for non-use of these medications, but in many cases the reasons for non-use were unidentifiable. Further studies are required to develop protocols or clinical pathways to improve the use of heart failure medications in particular ACE inhibitors and β-blockers.

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