International Journal of Cardiovascular Research
Review Article

Prevalence of Prescribing Contraindications in Chronic Heart Failure Patients

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Received: 25 June, 2019; **Accepted**: 31 August, 2019; **Published**: 07 September, 2019

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Abstract

Introduction

Chronic heart failure (CHF) affects at least 26 million people worldwide causing significant morbidity and mortality. Noncompliance with heart failure prescribing guidelines is well documented in the literature in both primary and tertiary settings. The primary aim of this study is to evaluate the proportion of patients who are prescribed pharmacological therapy contraindicated in patients with CHF on discharge at this Australian hospital. The secondary aims are to examine the proportion of patients prescribed contraindicated medications on discharge on cardiac wards compared to medical wards, to assess pharmacist input on prescribing patterns and to explore predictors of prescribing patterns in these patients.

Method

A cross sectional studies of patients admitted for management of CHF has been conducted over a 6 month period. The data collected from the case notes included patient's age, gender, comorbidities, medications, discharge wards, as well as pharmacist input.

Results

A total of 618 patients fulfilled the inclusion criteria and were included in the study. A total of 140 (23%) were prescribed medications on discharge that were contraindicated in CHF. Steroids were the most commonly contraindicated drug class prescribed in CHF patients on discharge accounting for 72% of all medications prescribed on discharge followed by non-dihydropyridines calcium channel blockers (21%), and Tricyclic antidepressants (19%). Patients discharged from medical wards had a higher prevalence of prescribing contraindications than those discharged from cardiac wards cardiac wards, $p<0.017$. Moreover, fewer patients were discharged on contraindicated medications in CHF when they had a pharmacist input during their admission compared to those who did not have a pharmaceutical (21% *vs* 26%, p=0.114). Predictors of appropriate prescribing patterns included, older patients (age>70) (OR=0.986 95% CI 0.630-1.544), admission to cardiac wards (OR=0.533 95% CI (0.309-0.918), as well as patients with end stage heart failure (OR=0.921 95% CI (0.105-8.503))

Conclusion

This pilot study identified gaps in prescribing practice for patients with CHF. It also demonstrated that patients admitted to cardiac wards and those who receive a pharmacist input during their inpatient stay receive treatment that is concordant with current prescribing guidelines. Further research is needed to explore reasons for non adherence to prescribing recommendations.

Keywords: Chronic Heart Failure; Prescribing Guidelines; Cardiac Wards; Hospital; Pharmacist Input

Highlights

- There is a prevalence of prescribing contraindications among CHF patients.
- Patients who are admitted to specialist cardiac wards and those who have a pharmacist input during their hospital stay are discharged on medications concordant to prescribing guidelines for CHF.
- Improving awareness of prescribing guidelines and exploring reasons for noncompliance to prescribing guidelines is needed for future research.

Introduction

Chronic Heart failure (CHF) affects at least 26 million people worldwide and is increasing in prevalence [1]. Given the increase in the ageing population, the number of people with CHF diagnoses is likely to contribute to a dramatic rise in health costs expenditure [1]. CHF affects over 300,000 Australians, causing significant morbidity and mortality. Expenditure on CHF management in Australia is believed to cost more than $1 million a year [2, 3].

Heart Failure is a complex clinical condition characterized by the reduced ability of the heart to pump blood around the body [4]. Causes of heart failure are varied and include both structural and functional cardiac abnormalities of the heart. Functional abnormalities of heart failure include longstanding untreated or uncontrolled hypertension, atrial fibrillation, a history of coronary heart diseases, cardiomyopathies, and valvular heart disease [4]. CHF is characterized by symptoms such as shortness of breath and fatigue, and signs such as fluid retention [5]. Several drugs are well known to exacerbate heart failure [6]. They include Non-steroidal anti-inflammatory drugs (NSAIDs) including COX-2 inhibitors due to their salt and water retention effect as well as their contribution to impairment of renal function [4, 6]. Non-dihydropyridine calcium channel blockers (verapamil and diltiazem) are contraindicated in heart failure with reduced ejection fraction due to their negative inotropic effect. Antiarrhythmic drugs (except beta blockers and amiodarone) and tricyclic antidepressants (TCA) have pro-arrhythmic effect and should be used with caution in patients with CHF [4,6]. Corticosteroids also cause salt and water retention and should similarly be avoided in these patients [4,6].Pioglitazone is also well documented to contribute to worsening of heart failure and should not be used in these patients [7]. Additionally, moxonidine is contraindicated in patients with all classes of heart failure as it has been associated with increased mortality and adverse effects [8].

Noncompliance with heart failure prescribing guidelines is well documented in the literature in both primary and tertiary health settings [9-12]. Evidence suggests that incidence of prescribing contraindications in patients with CHF is prevalent, contributing to hospital related admissions, increasing disease burden, as well as increasing incidence of

all-cause mortality of these patents [7,13].

Improving the care of CHF patients can be achieved through better understanding of patients' demographics, management, and adherence to prescribing guidelines as well understanding of contributing factors for their disease progression. Data on the prevalence of prescribing contraindications in CHF patients in Australia has been scarce after the release of the most recent CHF guidelines [10].

To date, only a few studies have reported on the proportion of patients discharged on medications that are contraindicated in CHF in Australian hospitals leaving a gap in the literature addressing adherence to the current recommended prescribing guidelines [14-16]. It is anticipated that data collected from this audit in combination with existing evidence provide greater insights into the prevalence of prescribing contraindications in heart failure in Australian hospitals.

The primary aim of this study is to evaluate the proportion of patients who are prescribed pharmacological therapy contraindicated in patients with CHF on discharge at this Australian hospital. The secondary aims are to examine the proportion of patients who are prescribed contraindicated medications on discharge on cardiac wards compared to medical wards, to assess pharmacist input on prescribing patterns and to explore predictors of prescribing patterns in these patients.

Methods

A retrospective cross-sectional audit of 858 patients' histories was undertaken for a period of 6 months in a large teaching hospital. The inclusion criteria of this audit included patients with a discharge diagnosis of CHF as per the International Classifications of Diseases (ICD 10) coding for patients with congestive heart failure (150.0), left ventricular failure (150.1), or hypertensive heart disease with congestive heart failure (I11.0). The exclusion criteria included patients under 18 years of age, patients with a diagnosis of HFPEF, diastolic congestive heart failure (as documented in the patient's medical records by the treating team), pregnancy, or if the main reason for admission was not management of heart failure, or if there was incomplete documentations of patients' management. Patients with rheumatic heart failure, T86.22—heart transplant failure, I97.131—post procedural heart failure following other surgery, I97.130—post procedural heart failure following cardiac surgery, I13.0—hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease were also excluded. Furthermore, palliated or patients who died while inpatients were also excluded. The data collected from the case notes included patients' age, gender, comorbidities, medications, discharge wards, as well as pharmacist input. Pharmacist input was determined if there was a documented pharmacist intervention in the examined patients' medical case notes or documented pharmacist electronic verification of charts.

Statistical analysis

Analysis of data involved both descriptive, univariate, and multivariate statistics. Data were analyzed using SPSS, version 24.0 (SPSS, Inc, an IBM Company, Chicago, Illinois) and M plus V7.3. Descriptive statistics were used to summarize patients' demographics and prevalence of prescribing of contraindicated therapy. Chi-squared was used to examine the relationship between 2 categorical variables. A significance level of $P < .05$ or $P < .01$ was considered statistically significant for all tests. Multivariate logistic regression model was used to examine the relationship between the independent variables such as age, class of heart failure, admission ward as well as pharmacist input and the dependent variables on discharge on therapy contraindicated in heart failure such as (NSAIDS, COX2, Steroids, moxonidine, Non-dihydropyridines calcium channel blockers as well as steroids. The results are presented in adjusted odds ratios (OR) with 95% confidence intervals (95% CI).

Table (1) outlines predictors of prescribing patterns in CHF patients in this study.

	Age > 75 years of age OR 95%(CI)	Cardiac wards OR95%(CI)	Lack of Pharmacist Input OR 95%(CI)	Class 3 OR95%(CI)	Class 4 OR95%(CI)
Prescribed HF contraindicated medications on Discharge	0.986 (0.630-1.544)	0.533 (0.309-0.918)	1.420 (0.938-2.150)	2.297 (0.271-19.439)	0.921 (0.105-8.053)
P value	0.951	0.023	0.097	0.445	0.941

Ethics approval was obtained from the hospital Research and Ethics committee. Ethics application reference number is QA/13/PH3.

Results

A total of 858 heart failure patients were admitted consecutively to this Australian hospital with a primary diagnosis of CHF over a 6 months period. A total of 240 patients were excluded due to various reasons such as a diagnosis of a different type of heart failure other than CHF, decision to palliate the patient, inpatient mortality, or incomplete documentation in the patients' case notes.

A total of 618 patients fulfilled the inclusion criteria and were included in the study. A total of 342 patients were coded for admission ICD150.0 (congestive heart failure), 256 patients were coded for ICD150.1 (Left ventricular failure), and 20 patients were coded with ICD111.0 (hypertensive heart failure with congestive heart failure). The mean age of patients reviewed was 78.9 ± 11.7 years. There were 320 (52%) females and 298 (48%) males. The 3 most prevalent comorbidities were hypertension (66%), respiratory conditions (such as asthma and Chronic Obstructive Pulmonary Disease (COPD)) (54%), atrial fibrillation (52%) and kidney disease (44%) which are predisposing factors to heart failure. Refer to (Table 2).

A total of 133 (22%) patients admitted with a diagnosis of CHF were treated on cardiac wards. Patients admitted to cardiac wards had a higher percentage of cardiovascular comorbidities compared to those admitted to medical wards. These included; a history of acute myocardial infarction (AMI) (48% cf 33%, $p=0.329$) and valvular disease (38% cf 22%, $p<0.05$). On the other hand, patients who were admitted to medical wards had a higher percentages of medical comorbidities such as COPD (42% cf 21%,$p<0.05$) and kidney disease (47% cf 33%, $p<0.05$).

About 99% of all the admitted patients were classified to have type III or IV heart failure class according to the NYHA classifications. There was no statistical significance between the severities of heart failure disease class between patients admitted to cardiac or medical wards. Refer to (Table 2).

Table (2): outlines study patients 'demographics and comorbidities

Parameter	N=618	Cardiac ward N=133	Medical wards N=485	P value, difference Between cardiac and medical wards
Patients Age (years)	Mean=78.9 ± 11.7 years, 88% aged>55 years	Mean age =71.9 ± 13.9 Years	Mean age = 80.9 ± 10.2 Years	P=0.001
Male (M) to Female (F) ratio		1.5	0.8	
Patients co-morbidities				
Hypertension	406 (66%)	81 (61%)	325(67%)	P=0.215
Atrial Fibrillation	321 (52%)	64(48%)	257(53%)	P=0.329
Kidney Disease	271 (44%)	44(33%)	227(47%)	P<0.05
Chronic Obstructive Pulmonary Disease	232 (38%)	28(21%)	204(42%)	P<0.05
Ischaemic Heart Diseases	230 (37%)	53(40%)	177(36%)	P=0.480
Acute myocardial infarction (AMI)	225(36%)	64(48%)	161(33%)	P<0.05
Diabetes Mellitus	216(35%)	53(40%)	163(34%)	P=0.814
valvular disease	158(26%)	51(38%)	107(22%)	P<0.05
asthma	100(16%)	17(13%)	83(17%)	P=0.287
NYHA classes at admission				
I	0(0%)	0(0%)	0(0%)	P>0.05
II	7(1%)	1(0.8%)	6(1%)	P>0.05
III	429(69%)	87(65%)	342(70%)	P=0.288
IV	182 (29%)	45(34%)	137(28%)	P=0.238

Prescribing contraindications

A total of 140 (23%) were prescribed medications on discharge that were contraindicated in heart failure. Steroids were the most commonly contraindicated drug class prescribed to CHF patients on discharge accounting for 72% of all medications prescribed on discharge followed by non-dihydropyridines calcium channel blockers (21%), TCAs (19%), and moxonidine (5%).

Other classes of medications included: NSAIDS, pioglitazone and antiarrhythmic agents which accounted for 2% of all contraindicated medications that were prescribed on discharge in these patients.

A larger number of patients (N=120 (24%)) who were discharged from medical wards had a higher prevalence of prescribing contraindications Compared to those who were discharged from cardiac wards (N=20, 17%) p<0.017. Refer to (Table 3).

Table (3): Percentages of patients discharged on HF contraindicated when admitted to the cardiac wards compared to the medical wards, in compliance with the Australian National Heart failure Guidelines.

	Total number of contraindicated medications per drug class N=618	Cardiac wards Number and % of patients discharged on medications N=133	Medical wards Number and % of patients discharged on medications N=485	P Value
Moxonidine	7(1%)	1(1%)	6(1%)	
NSAIDS/COX2	1(<1%)	0(0%)	1(0%)	
Cal Channel Blockers	29(21%)	2(2%)	27(6%)	
TCA	27(19%)	11(8%)	16(3%)	
Steroids	101(72%)	9(7%)	92(19%)	
Pioglitazones	1(<1%)_	1(1%)	0(0%)	
Anti-arrhythmic drugs	1(<1%)	0(0%)	1(0%)	
Total number of contraindicated drugs	140(23%)	20(17%)	120(24%)	P<0.017

Pharmacist input

A total of 436 (71%) patients were reviewed by a clinical pharmacist during their admission. In this cohort, fewer Patients were discharged on contraindicated medications in CHF compared to those who were not reviewed by a pharmacist on discharged (21% *vs* 26 %, p=0.114). Refer to table 4.

Table (4) Percentages of patients who were discharged on inappropriate medications in CHF with respect to pharmacist input

	No Pharmacist input N=182(29%)	Pharmacist input N=436(71%)	P value
Total number of patients discharged on contraindicated drugs in CHF	48(26%)	92(21%)	P=0.114

Predictors of prescribing patterns in chronic heart failure

This pilot study identified that older patients (age>70) (OR=0.986 95%CI(0.630-1.544), admission to cardiac wards (OR=0.533 95% CI (0.309-0.918), patients with NYHF stage 4(OR=0.921 95%CI (0.105 -8.503) were less likely to be discharged on medications that are contraindicated in CHF However, the results did not reach statistical significance for these factors, p>0.05. Additionally, patients whose medications were not reviewed by a pharmacist during their admission or at discharge were more likely to be discharged on contraindicated therapy (OR=1.420 95% CI (0.938-2.150), P=0.097. Refer to Table 1.

Discussion

Assessing prevalence of prescribing contraindication in patients with CHF was a key objective of this study. Optimal management of CHF patients has been shown to improve patients' morbidity and reduce their mortality. Given the patients' demographics and existing comorbidities', it is not uncommon that poly pharmacy is prevalent in this patient group [13].

This pilot study identified that close to a quarter (23%) of the patients that were eligible to be included in this cohort had contraindicated medications in CHF prescribed to them on discharge. This study showed that prescribing contraindications were more prevalent on medical wards than cardiac wards (24% cf 17%, $p<0.017$). Predictors of appropriate prescribing included older patients, admission to specialized cardiac wards, end stage disease (class 4 NYHF) as well as pharmacist input.

Steroids (72%) were the most common class of medications prescribed in these patients. Although steroids play a limited use in patients with cardiac disease, they however have a role in the management of myocarditis. Steroids are contraindicated in CHF due to their fluid retention activity resulting in increased peripheral resistance; however, agents such as prednisolone and prednisone have a less marked influence on sodium retention. Nonetheless, recent prescribing guidelines contraindicate their use in patients with CHF [17]. Current evidence suggests that these agents increase risk of hospitalization as well as all-cause mortality in CHF patients [18].

Non-dihydropyridines calcium channel blockers accounted for 21% of all drugs that were prescribed inappropriately. Non dihydropyridine calcium channel blockers have a negative inotropic effect on the heart and can worsen heart failure. The Multicenter Diltiazem Post infarction Trial Research Group has demonstrated that Diltiazem increased the risk of cardiac events as well as pulmonary congestion in these patients [19].

TCAs were the third most frequent contraindicated medications prescribed in the audited patients in this study. They represented 19% of all medications that were prescribed inappropriately in CHF patients in this pilot study. TCAs have a wide range of cardiovascular adverse effects including sinus tachycardia, proarthrymthic effect, second and third degree heart block as well as postural hypotension [20]. Additionally, cardiomyopathy has been reported in patients with reduced Ejection fraction within weeks or years of taking TCAs [21, 22].

Despite several published studies showing prescribing contraindications in heart failure attribute to patients harm, contraindicated medications are still being prescribed at similar rates across multiple settings as evidenced by the findings in this pilot study [18-23]. Prevalence of inappropriate prescribing on discharge in this cohort of CHF patients was in line to recently published literature (23% *vs* 22%, $p=0.114$) [23]. Similar to this study, a recent study published by Caughey et all has also identified that systemic corticosteroids (17.4%), TCAs and NSAIDs (6.2%) are also the most frequent contraindicated medications prescribed in a cohort of 4069 heart failure patients [23]. Moreover, several studies have shown that patients' comorbidities are a major factor for inappropriate prescribing in heart failure [24, 25]. Similarly, a large percentage of this cohort (54%) had a documented diagnosis of COPD or asthma explaining the high rate of steroid prescribing pattern identified in this study.

Multiple studies have also shown that patients on cardiac wards are better managed according to prescribing recommendations than those who are admitted to medical wards [9, 26, 27]. Data from this pilot study is also consistent with this well published findings. Patients admitted to cardiac wards had a lower level of inappropriate prescribing compared to those admitted to the medical wards (17% *vs* 24%, $p<0.017$), highlighting a gap in prescriber's awareness of clinical guidelines, clinical judgments or perhaps

assumption for follow-up of patients by their primary health physicians for further optimization of their management.

Furthermore, pharmacists play an instrumental role in optimizing patients' medical management of heart failure [9, 28-31]. They utilize their extensive drug and therapeutics knowledge to monitor for adherence to prescribing guidelines, identify drug-drug and drug disease interactions as well as monitor adverse effects [9, 28-31]. This was also demonstrated in this study by the lower percentage of patients who were reviewed by pharmacists and were prescribed medications deemed to be contraindicated in heart failure (21% *vs* 26%). The results presented in this pilot audit highlighted the importance of including pharmacists as an integral part of a multidisciplinary team especially for management of patients with chronic diseases.

Finally, results from this pilot audit demonstrated the benefit of managing chronic disease patients on specialized wards, as well including a pharmacist as part of a multidisciplinary team for management of these complex patients in the aim of providing better quality of life for patents with late stage CHF (stage 3 and 4 NYHF). Additionally, this study highlighted some variances in physicians' management of CHF and offers opportunities for further research to explore reasons for differences observed in the management of such a common condition that contributes to a large economic and personal burden to our society and to the patients involved.

Limitations of this study included lack of determining patients' choice in their management, or identifying other herbal or over the counter medications that are contraindicated in heart failure. Failure to consider any of these factors would underestimate the prevalence of prescribing contraindications in heart failure. Additionally, likelihood of harm or rehospitalisation on patients who were discharged on contraindicated medications in heart failure could not be determined. A pharmacist selection method for prioritizing review of patients was not explored and hence their input could have contributed to selection bias.

Conclusion

This pilot study identified gaps in prescribing practice for patients with CHF. It also demonstrated that patients admitted to cardiac wards and those who receive a pharmacist input during their inpatient stay receive treatment that is concordant with current prescribing guidelines. Further research is needed to explore reasons for non adherence to prescribing recommendations.

Acknowledgments

The author would like to thank Melanie Danninger for her assistance with data collection.

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