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Use of an indicator to evaluate physician adherence to prescription guidelines for the treatment of heart failure

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The aim of this study was to use indicators to evaluate physician adherence to prescription guidelines for heart failure treatment in a university hospital. This was a prospective cohort study conducted in a university hospital. The information collected at the time of patient admission, including therapeutic indication, absolute contra indications and intolerance, was utilised for the formulation of a guideline adherence indicator (GAI). This indicator was calculated as follows: (the number of patients who used the medication/the number of eligible patients) x 100. The percentage of eligible patients was calculated using the following formula: (the number of eligible patients/the total number patients) x 100. The GAI was applied to a population of 53 patients. Inhibitors of angiotensin-converting enzyme/angiotensin receptor blocker (ACE-I/ARB) combination therapy were used in the greatest percentage of eligible patients (92.4%) and demonstrated the largest GAI value (73.5%). The percentages of patients who were eligible for beta-blockers, spironolactone and digitalis treatments were 81.1%, 52.8% and 60.4%, respectively. The GAI values for the use of beta-blockers, spironolactone and digitalis were 60.4%, 57.1% and 56.2%, respectively. For the studied patient population, the GAI was consistent with the proportion of patients who were eligible to receive digitalis and spironolactone.

Uniterms: Heart failure/treatment. Health care. Clinical medicine/practice guidelines. Medicines/use. Medicines/prescriptions.

O objetivo deste estudo foi utilizar indicadores para avaliar a adesão de médicos às diretrizes para tratamento da Insuficiência Cardíaca em um hospital universitário. Estudo de coorte prospectivo, conduzido em um hospital universitário. As variáveis coletadas na admissão do paciente foram: indicação terapêutica, contraindicações absolutas e intolerância, sendo utilizadas para elaboração de um indicador de adesão à diretriz (IAD). Este indicador foi calculado através da relação: (número de pacientes que utilizaram o medicamento/número de pacientes elegíveis) x 100. A % de pacientes elegíveis foi calculada da seguinte forma: (número de pacientes elegíveis/número total de pacientes) x 100. Os IAD foram aplicados para uma população de 53 pacientes. Os Inibidores da Enzima Conversora de Angiotensina/ Bloqueadores dos Receptores de Angiotensina foram as classes farmacológicas que apresentaram maior % de pacientes elegíveis (92,4%) e apresentaram o melhor IAD (73,5%). A % de pacientes elegíveis para beta-bloqueadores, espironolactona e digitálicos foi de 81,1%, 52,8% e 60,4%, respectivamente. O IAD para beta-bloqueadores foi 60,4%, espironolactona 57,1% e digitálicos 56,2%. Na população estudada, o IAD foi compatível com a proporção de pacientes elegíveis para digitálicos e espironolactona.

Unitermos: Insuficiência cardíaca. Assistência à Saúde. Clinica médica/guia prático. Medicamentos/ uso. Medicamentos/prescrição.

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INTRODUCTION

Heart failure (HF) is a major health problem associated with high levels of morbidity and mortality (Komajda *et al.*, 2003). Furthermore, it is estimated that 30% of patients are re-hospitalised within the first year of diagnosis and that the 5-year mortality rate may be greater than 50% (Ho *et al.*, 1993). The therapeutic objectives for the treatment of HF are focused on improving the patient's quality of life, alleviating or reducing symptoms, preventing hospitalisation, slowing the progression of the illness and increasing the survival rate. The use of angiotensin-converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs) and beta-blockers (BBs) has shown a reduction in the mortality and hospital admission rates for patients with HF, and the greatest benefit of these therapies has been for patients with severe HF (Bocchi *et al.*, 2009). Based on these findings, various professional associations have developed guidelines for the assessment and treatment of HF (Bocchi *et al.*, 2009). In Brazil, the Brazilian Society of Cardiology (BSC) published a set of guidelines in 2009 (Bocchi *et al.*, 2009).

Certain international organisations suggest the use of quality indicators for the treatment of HF because multiple studies have shown that published guidelines are commonly not followed, especially regarding medication selection and the dosage used (Drechsler *et al.*, 2005). In addition to the underutilisation of recommended medications, polypharmacy often occurs in the treatment of HF. Moreover, the difficulty of accessing data from recent clinical trials may further hinder physicians' ability to manage HF treatment (Komajda *et al.*, 2003). Additionally, studies have shown that physician adherence to prescription guidelines for HF treatment has improved the prognosis for related pathologies (Komajda *et al.*, 2003). According to the results of the MAHLER study, good physician adherence to HF treatment guidelines, as assessed using indicators, was associated with a reduction in the 6-month hospitalisation rate (Komajda *et al.*, 2003). These indicators accounted for criteria regarding the use of various HF medications, as published in the guidelines of the European Society of Cardiology (ESC). Subsequently, two additional studies utilised national or recently developed guidelines from the ESC for the development of similar evaluations (Peters-Klimm *et al.*, 2007; Störk *et al.*, 2008).

The aim of this study was to use indicators to evaluate physician adherence to prescription guidelines for HF treatment in a university hospital.

METHODS

The Study for the Identification of Treatable Causes and Therapeutic Optimisation of Heart Failure (SITCO) is an observational study with the main objectives of identifying the treatable causes of decompensation and the need for hospitalisation due to HF and evaluating the frequency and appropriateness of medication use for HF pathology. A prospective cohort of patients hospitalised for HF was treated at a Brazilian university hospital. The data were collected during patient admission and stay at the hospital using a standard survey, an interview and the review of medical records. The data sources included the prescriptions prior to hospitalisation and the diagnoses during the patient's stay at the hospital during the period from July 2009 to December 2010. The SITCO included patients with decompensated HF but excluded those with untreatable concomitant disease and an estimated life expectancy of less than one year.

A version of the guidelines that were developed by the MAHLER study was used to calculate the guideline adherence indicator (GAI) *(*Komajda *et al.,* 2005). The criteria regarding contraindications established in this study were adapted for a Brazilian context, and these criteria were in agreement with the medication criteria established by the III Brazilian Guidelines for Chronic Heart Failure (Komajda *et al.*, 2005). The GAI that was used considered the indications for each drug, the absolute contraindications, the intolerance indications and other clinical situations that would require greater precautions to be made for the clinical management of patients. Criteria for drug use (indications and contraindications) were extracted for each pharmacological group, including the ACE-I, ARB, aldosterone antagonist and BB treatments, based upon information in the Brazilian guidelines (Bocchi *et al.*, 2009). The data were transformed into eligibility criteria for treatment with a given medication, which were then compared to the clinical data and the data regarding treatment at the time of hospital admission (Table I). Patients eligible for treatment for heart failure were those with indications for each drug, no absolute contraindications, intolerance or other medical conditions which require greater precautions in clinical management.

The term adherence in this study refers only to the comparison of the prescribed treatment within the guideline recommendations. The percentage of eligible patients was calculated in the following manner: (the number of eligible patients/the total number of patients) x 100. The GAI was calculated based on the following

TABLE I - The general eligibility criteria for HF treatment according to therapeutic class and based on the national guidelines

Therapeutic class	National guideline recommendations	Contraindications
ACE-I or ARB	EF ≤40% independent of symptoms	Bilateral renal artery stenosis, K^+ >5.0 mmol/L, Cr >2.5 mg/dL, serious aortic stenosis, symptomatic hypotension, cough, pregnancy/breastfeeding, hypersensibility, cardiogenic shock
Beta-blockers*	**LVEF** <40% and HF II-IV, asymptomatic after MI with dysfunction of LV, clinical stability	Asthma, serious COPD, bradycardia <5, Second- and third-degree AV block, sinus node disease, symptomatic hypotension, hemodynamic repercussion with valvular disease, cardiogenic shock, life expectancy less than one year, liver failure, decompensated HF, hypersensibility.
Aldosterone antagonists	**LVEF** <35%, HF III-IV, BB and optimised ACEI/ARB	K^+ >5.0 mmol/L, Cr >2.5 mg/dL, use of ACE-I+ARB, hypersensibility.
Digitalis	AF with RV >80 bpm, sinus rhythm with symptoms (HF II-IV), optimised dose of ACE-I/ARB, BB and spironolactone.	Second- and third-degree AV block, pre-excitation, symptomatic bradycardia without pacemaker, intolerance to digitalis.

*Except for metoprolol tartrate, propranolol and atenolol; LVEF - left ventricular ejection fraction; AF - atrial fibrillation; BB - beta-blocker; COPD - Chronic Obstructive Pulmonary Disease; MI - Myocardial infarction.

ratio: (the number of patients who used the medication/ the number of eligible patients) x 100. Deaths were excluded from both calculations, because for these patients was not possible to investigate all the possibilities of contraindications or intolerance or even confirmation of indication for each drug. Therefore, these patients died before a complete clinical investigation. For each therapeutic class that was recommended in the clinical guidelines, there was one corresponding GAI that could vary between 0 and 100%. Because evidence for the benefits would be stronger for the use of ACE-I, BBs or spironolactone than for digitalis, a separate GAI was calculated based upon the set of these three classes (GAI-3) (Komajda *et al.*, 2005).

The GAIs for pharmacological class and the GAI-3 were calculated based on the data collected during the patients' hospital stays as well as the SITCO baseline data from 2010. The variables of interest included demographic data, the functional class according to NYHA, various laboratory data, co-morbidities (such as atrial fibrillation, coronary disease, hypertension, asthma, chronic obstructive pulmonary disease and renal failure) and the HF medications used (including BBs, ACE-I or ARB, digoxin and spironolactone).

The results were analysed using SPSS 11.0 software and are shown as the mean ± standard deviation for continuous variables or as frequencies for dichotomous variables. All data referring to the medications administered were stratified according to pharmacological class. The SITCO was approved by the local ethics research committee.

RESULTS AND DISCUSSION

The GAI was applied to a population of 53 patients. The most common aetiology for HF was Chagas disease (37.7%). The majority of patients (80.3%) had been given a previous diagnosis of HF prior to their admission to the hospital, and 44.3% of these patients had been admitted with serious ventricular dysfunction (Table II).

The most commonly prescribed pharmacological drug classes upon admission were the ACE-I and ARB medications (68.8%), which demonstrated the best GAI values (73.5%). However, the combination of these medications with either BBs or spironolactone led to a GAI of 40.7% (Table III).

We found a GAI of 40.7% for the combination of ACE-I/ARB, BBs and spironolactone. For the individual pharmacological classes, the GAI varied from 52% to 73.5%.

The frequency of patients who receive ACE-I or BBs at the routine and appropriate doses is regarded as a quality indicator for HF treatment (Pereira Barretto *et al.*, 2001). Since 1997, the routine use of ACE-I/ARB has been recommended for the management of HF cases due to left systolic ventricular dysfunction (Komajda *et al.*, 2003; Drechsler *et al.*, 2005). The combined use of these medications with diuretics has resulted in patients being less symptomatic with lower degrees of decompensation, less hospitalisation and lower mortality rates from this disease (Pereira Barretto *et al.*, 2001). Studies have also shown a decrease in mortality among patients who have left ventricular dysfunction and have been treated with

TABLE II - Patient characteristics (N = 61)

Characteristics	
Age (M ± SD)	57.1 ± 14.3
Male n (%)	34 (55.7)
Aetiology n (%)	
Chagas	23 (37.7)
Idiopathic	12 (19.7)
Ischemic	10 (16.4)
Hypertensive	7 (11.5)
Valvular	6 (9.8)
Others	3 (4.9)
Previous diagnosis of HF n (%)	49 (80.3)
Serious ventricular dysfunction (LVEF <30%) n (%)	27 (44.3)
Duration of hospital stay in days (M±SD)	23.1±19
Admitted to ICU n (%)	24 (39.3)
Use of vasoactive drugs n (%)	19 (31.1)
Comorbidities n (%)	
Hypertension	35 (57.4)
Diabetes	14 (23)
Asthma	2 (3.3)
COPD	5 (8.2)
Death n (%)	8 (13.1)

HF - Heart failure; LVEF - Left ventricular ejection failure; ICU - Intensive Care Unit; COPD - Chronic Obstructive Pulmonary Disease.

aldosterone antagonists (Pereira Barretto *et al.*, 2001). The DIG study revealed that hospitalisation due to worsening of the disease decreased by 28% in the group that was treated with digoxin (The effect of digoxin on mortality and morbidity in patients with HF. The Digitalis Investigation Group, 1997).

The GAI was also used in three previous European studies that assessed the quality of care in patients with HF (Störk *et al.*, 2008). However, only two of these studies considered contraindications and patient intolerance when establishing the eligibility criteria for HF treatment (Störk *et al.*, 2008). The first study reported that after adjusting for potential contradictions (COPD, heart rate <60/min, hypotension, hyperkalaemia and renal dysfunction), adherence appeared to be 49% for ACE-I/ARB treatments and 46% for BB treatments. Aldosterone antagonists were prescribed for 57% of cases, whereas the prescription rate for triple therapy (ACE-I/ARB + BB + AA) was only 25% for 83 indicated cases (Peters-Klimm *et al.*, 2007). The second study reported that the median GAI-3 was 67% for patients with a reduced LVEF (Störk *et al.*, 2008).

The current study used an identical methodology and adapted these criteria for use with the Brazilian guidelines. Numerous studies have described only the prescription frequencies of these medications without considering the possible contraindications or intolerances (Boyles *et al.*, 2004; Adams *et al.*, 2005; Jaarsma, *et al.*, 2005). As a result, this approach may have led to a misinterpretation of the quality of care provided, given that each of these studies indicated the underutilisation of medications that have been proven to be beneficial in large clinical trials and have been disclosed in national and international guidelines.

In Brazil, few studies have evaluated the appropriateness of medication prescriptions for patients with HF or demonstrated the underutilisation of BBs and ACE-I treatments at lower than the recommended doses (Pereira Barretto *et al.*, 2001). In a Brazilian survey, a questionnaire was used to compare the perceptions regarding diagnosis with the management of HF among clinical cardiologists and family physicians. The doses of ACE-I medications that were issued by the cardiologists were greater than the doses issued by family physicians, although the doses of spironolactone were closer to those

TABLE III - Proportion of patients with medications for HF at the time of admission, eligible patients and the GAI for each pharmacological group

Therapeutic class	Per cent of patients with prescription at admission (n/N)	Per cent of eligible patients (n/N)	GAI (%) [n/N]
ACE-I/BRA	68.8 (42/61)	92.4 (49/53)	73.5 [36/49]
BB	54.1 (33/61)	81.1 (43/53)	60.4 [26/43]
Spironolactone	49.2 (30/61)	52.8 (28/53)	57.1 [16/28]
Digitalis	44.3 (27/61)	60.4 (32/53)	56.2 [18/32]
Diuretics	67.2 (41/61)	-	-
(ACEI/ARB)+BB+ Spironolactone	32.8 (20/61)	50.9 (27/53)	40.7 [11/27]*

*GAI-3. ACE-I - angiotensin-converting enzyme inhibitors; BB - beta-blocker; ARB - angiotensin receptor blocker

recommended in the literature (Pereira Barretto *et al.*, 2001). In another Brazilian study, the underutilisation of ACE-Is (64.1%) and BBs (41.1%) was demonstrated in primary care patients. The most commonly used BBs included propranolol and atenolol, which have not been shown to provide benefits for patients with HF (Moscavitch *et al.*, 2009). These studies were based upon data from the guidelines of the BSC for assessing prescriptions and were limited to describing the frequency of use of pharmacological agents.

In the current study, approximately 20% of the patients evaluated had not been given a previous diagnosis of HF, and this fact may have contributed to the underutilisation of medication in these patients. For the ACE-I/ARB medications and BBs, the proportion of eligible patients was greater than 80% for each class (92.4% and 81.1%, respectively). However, only the appropriateness of use regarding the ACE-I/ARB medications surpassed data from previous studies.

The number of patients with a LVEF <30%, the severity of the cases requiring admission to the ICU and the use of vasoactive drugs suggest that specific groups of patients may not be able to tolerate the use of BBs, which were the pharmacological class with the lowest GAI in the studied population. The respective GAIs for spironolactone and digoxin were similar to the proportion of eligible patients. The combined use of ACE-I/ARB medications with BBs and spironolactone also had a GAI that was similar to the proportion of eligible patients. These results support the hypothesis that a simple description regarding the existing data on medication use for patients with HF that does not account for the clinical aspects of treatment could yield false evidence for the underutilisation of these medications.

The present study provided an opportunity for clinical practitioners who are not affiliated with a teaching hospital to communicate with general practitioners who attend to patients with HF in the community, regardless of their specialty. Because these data originated from hospital admissions, additional medications could have been introduced later during the hospital stay. However, analysis of the data from SITCO during the patients' stay at the hospital would permit us to evaluate whether the therapy was optimised during the period of hospitalisation.

The SITCO study includes a population of heart failure patients hospitalized in the study institution. No sample was taken. As it comes to hospitalization of patients with HF in a specialized unit, the authors believe that the data presented are useful for clinical practice, although not a random sample. Even if it was a random sample, statistical inference would come down to the institution of study.

The methodology for the use of the GAI may be useful for assessing with greater accuracy whether there is underutilisation of certain therapeutic classes of drugs for the treatment of HF, given that certain contraindications are very common in patients with COPD, kidney disease, hyperkalaemia and other conditions. Therefore, the GAI approach should be preferentially used for studies with institutional data involving thousands of patients.

Using the criteria related to medication use that are based on national guidelines and applying the GAI approach to a population of hospitalised patients with HF revealed that this strategy could accurately define standards for the quality of care of these patients. This strategy also accounts for the eligibility regarding the use of each specific treatment. The use of the GAI for patients with HF was shown to be an easily applied tool that is capable of aiding the monitoring of care in both outpatient and hospitalised patients. Furthermore, in the studied population, the GAI for each selected medication was not consistent with the proportion of patients who were eligible for treatment with BBs and ACE-I/ARB medications.

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