Heart Failure Treatment Profile at the Beta Blockers Era

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Summary

Objective: The inhibition of the rennin-angiotensin-aldosterone system (RAAS) and sympathetic autonomous nervous system has increased the perspective of survival in these patients, as well as allowing the improvement of the quality of life. The aim of this study was to evaluate the reality of the treatment employed and its impact on the disease in patients followed at a specialized heart failure (HF) outpatient clinic.

Methods: A sample of 96 patients followed at the HF and Transplant Outpatient Clinic of Heart Institute of the University of São Paulo School of Medicine (InCor - HCFMUSP) were evaluated. The data were collected during the ambulatory consultation from the medical files and through physical examination. Patients were randomly selected for the study.

Results: Most of the patients were Functional Class II (42.3%) and evolution stage C (94.9%). The medical prescription given to the patients was quite similar to the one recommended by the directives. Approximately 95% of them received RAAS inhibitors (ACE inhibitor – enalapril and captopril – or angiotensin receptor antagonist – losartan), whereas 85% of the patients additionally received beta blockers (carvedilol). The mean dose prescribed was also similar to the one used in large studies and reached more than 60% of the maximum dose for each medication. The hemodynamic data show that patients were stable, despite the intensity of the dysfunction and ventricular remodeling observed in these patients.

Conclusion: Patients with HF followed by a specialized medical team receive a medical prescription that is closer to the recommended one. These patients, despite the marked characteristics of disease severity, achieve hemodynamic and clinical stability with an adequate therapeutic optimization.

Key words: Cardiac output, low heart failure, outpatient clinic hospital, renin-angiotensin system.

Introduction

Heart failure (HF) currently represents one of the most prevalent diseases of the cardiovascular system, resulting in elevated social and economic costs. In the United States there are currently 5 million people with the disease, with 550,000 new cases diagnosed every year[1]. In Brazil, decompensated HF is responsible for 3.18% of hospital admissions and 6.97% of deaths of these patients. It also corresponds to 19.6% of hospital admissions due to cardiovascular causes, which comprehends 11.7% of all hospital admissions in the country[2].

In the last two decades there has been remarkable progress in the treatment of HF. The introduction of beta blockers and the rennin-angiotensin-aldosterone system (RAAS) has caused a noticeable change in the patients' clinical behavior, as well as brought a perspective of more promising survival rates. Large studies have shown important reductions in mortality[3-7], as never before seen in the treatment of HF.

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However, the possibilities of therapeutic and clinical optimization have had to face patients' low adherence and the physicians' reluctance in prescribing certain medications[8]. Several small studies showed the low incidence of prescription of medications recommended by international directives; in Holland, for instance, the prescription of angiotensin-converting enzyme inhibitor (ACEI) reaches 60%, whereas beta blockers are prescribed to up to 37% of the patients[9]. It is estimated that 57% of the hospital admissions due to HF could be prevented with better therapeutic adherence[10].

Coupled with undertreatment, the underdose does not allow reaching the results obtained in the large studies[11].

Other studies have demonstrated better clinical results in populations with better treatment adherence. Flesh et al[12] have demonstrated that 63% of the German patients with HF continuously use ACEI, angiotensin receptor blocker (ARB) and beta blockers. These patients presented a decrease of 40% of hospital admissions due to decompensated HF.

Recently the HF clinics, which are multidisciplinary units with professionals that are specialized in the disease, have been able to improve patients' adherence not only to the drug therapy but also to the restriction of salt intake and other non-pharmacological measures. These life style changes have

allowed improvement in patients' survival rates and quality of life[13].

The present study aimed at improving the knowledge on how HF is treated in a specialized outpatient clinic in a quaternary hospital. Additionally, the patients' clinical data, comorbidities and data related to the disease were also assessed.

Methods

All of the patients enrolled in the study are currently being followed at the Heart Failure and Transplant Outpatient Clinic of Instituto do Coração of Hospital das Clinicas of the University of São Paulo School of Medicine (InCor- HCFMUSP). The HF outpatient clinic of InCor follows patients with ventricular dysfunction at different stages of evolution, from asymptomatic ones to those being prepared for heart transplant. Patients who have undergone heart transplant at our institution are also followed there. The medical team consists of 5 assistant physicians, residents in cardiology and physicians specializing in HF. The consultation dynamics is carried out by the resident physicians, followed by the discussion of each patient's case with the assistant of the shift. Approximately 36 previously scheduled consultations take place daily.

Patients were randomly selected for the present study. During a period of 6 weeks, the first 3 patients seen at the outpatient clinic were selected for the study, which was known only at the moment of the consultation. The data were collected during the consultation from the medical files (laboratory results, electrocardiogram, echocardiogram and disease evolution) and from the patients' clinical examination (current clinical situation, currently used medications, hemodynamic data)

Results

The study showed that the mean interval between consultations was 4.3 ± 2.3 months. The studied group consisted of 36 women and 60 men. The patients were originally from the capital of the state of São Paulo (50.8%), the countryside of the state of São Paulo (38.9%) and from cities outside the state of São Paulo (10.1%). Table 1 shows the main characteristics of the studied group.

The mean hemodynamic data were: arterial systolic pressure: 120.9 ± 20.7 mmHg, arterial diastolic pressure: 77.7 ± 14.4 mmHg and heart rate: 71 ± 10.1 bpm.

Dissimilarly from literature data, which show low adherence to the recommended treatment for HF at the subanalysis of some studies, most of the studied patients was receiving optimized doses of medication or doses that were close to the ideal dose, according to the main established directives[14-16] (Table 2). RAAS inhibitors (ACEI – enalapril and captopril – and ARB – losartan) were prescribed to 94.7% of the patients, whereas the remainder received the combination hydralazine-nitrate combination due to renal failure. A total of 84.7% of the population received ACEI/ARB associated to a beta blocker (carvedilol). Regarding the use of beta blockers, among the 8.4% of the patients who were not using them, 5.2% had withdrawn the use due to clinical signs of intolerance to the drug (dizziness and hypotension), whereas the remainder presented contraindications to its use (bronchospasm and severe peripheral artery disease).

Table 1 - Characteristics of the studied patients

n	96
Gender (F/M)	36/60
Age (yrs)	52.4 ± 12.9
Weight (kg)	64.9 ± 12.2
Height (cm)	163.4 ± 9.9
BMI (kg/M²)	23.6 ± 5.0
Echocardiographic Data	
Posterior wall (cm)	0.83 ± 0.11
Septum (cm)	0.85 ± 0.15
LV Mass (g)	246.0 ± 90.3
Echocardiogram LVEF (%)	30.3 ± 11.6
LA (cm)	45.3 ± 12.3
LV (cm)	70.2 ± 10.0
Etiology (%)	
Idiopathic	28.2
Chagasic	8.6
Ischemic	28.2
Hypertensive	20.6
Tachycardiomyopathy	2.1
Valvular	6.5
Alcoholic	2.1
Peripartum	3.2
Comorbidities (%)	
Diabetes mellitus	20.8
Chronic renal failure	15.6
Dyslipidemia	28.9
Hypothyroidism	9.3
Hyperuricemia	5.2
Functional class – AHA/ACC (%)	
A	0
B	3.5
C	94.9
D	1.6
Functional class – NYHA (%)	
I	32.3
II	42.3
III	25.4
IV	0

BMI - body mass index; LV- left ventricle; LVEF - left ventricle ejection fraction; LA - left atrium; LVDD - left ventricle diastolic diameter; AHA/ACC - American Heart Association/American College of Cardiology; NYHA - New York Heart Association.

Even though they were receiving optimized medication for HF, 11.4% of the patients also received anti-hypertensive drugs (arterial vasodilators – hydralazine – and calcium channel antagonists – amlodipine and diltiazem). A total of 18.9% of the patients also received anticoagulants (warfarin), with 10.4% of them due to permanent fibrillation or atrial flutter.

Table 2 shows the prescribed dose/target dose ratio of the medication used (according to the main directives[14-16]) at the moment of the consultation. The standard doses adopted were: captopril 150 mg/day, enalapril 40 mg/day, losartan

Table 2 - Prescribed medications and mean doses

Medications being used (% de patients)	
ACEI	79.1
ARB	15.6
Beta-blocker	91.6
Diuretics	83.3
Digoxin	58.3
Spironolactone	53.1
Hydralazine – Nitrate	7.2
Mean daily dose (mg/day)	
ACEI	
captopril	92.1 ± 39.7
enalapril	30.8 ± 12.2
ARB	
losartan	61.6 ± 24.7
Beta-blocker	
carvedilol	34.2 ± 20.6
Diuretics	
furosemide	53.4 ± 24.9
hydrochlorothiazide	27.7 ± 8.0
digoxin	0.21 ± 0.05
spironolactone	25.0
hydralazine – nitrate	114.5 ± 76.4 – 80 ± 20.5
Prescribed dose/target dose ratio (%)	
ACEI	
captopril	61.4%
enalapril	77%
ARB	
losartan	61.6%
Beta blocker	
carvedilol	68.4%

ACEI - angiotensin-converting enzyme inhibitors; ARB - angiotensin-receptor blocker.

100 mg/day and carvedilol 50 mg/day. All of the reported medications are standardized in the institution.

Other biochemical data were also assessed, as shown in Table 3.

Table 3 - Mean laboratory data of the studied population

Sodium (mEq/l)	136.7 ± 14.5
Potassium (mEq/l)	4.8 ± 4.0
Urea (mg/dl)	50.6 ± 25.4
Creatinine (mg/dl)	1.1 ± 0.5
Hemoglobin (g%)	13.5 ± 1.6
Cholesterol total (mg/dl)	178.9 ± 53.3
Triglycerides (mg/dl)	137.7 ± 84.0
LDL (mg/dl)	104.9 ± 35.1
TSH (micro UI/mL)	1.7 ± 1.2
Free T4 (ng/dL)	1.6 ± 0.3
Total T4 (ng/dL)	8.7 ± 2.3
Glycemia (mg/dl)	104.8 ± 29.4
Uric acid (mg/dl)	7.9 ± 2.9

LDL - low-density lipoprotein; TSH - thyrotrophic hormone.

Discussion

Some of the population data disclosed in Table 1 show the severity of the disease in the studied patients. The significant left ventricular dilation and the severity of its dysfunction are classically considered as predictors of a bad prognosis. Considering these markers, it was not surprising that most of the patients were considered Functional Class III (NYHA) and evolution stage C (ACC/AHA). The relative hemodynamic stability presented by these patients, despite the severity of the disease, is noteworthy and in this analysis, it is important to emphasize the role of adequate therapeutics for such stability to take place.

The prescription rate of medications indicated by the international consensuses and directives was quite relevant, especially ACEI/ARB and beta blockers, the main mortality-reducing agents. All of the patients studied used ACEI or ARB (the latter in situations when the patient presented persistent cough due to ACEI use) or were receiving a hydralazine and nitrate combination, specifically patients with chronic renal failure with serum creatinine levels > 2.5 mg/dl. The use of ACEI and ARB combination, still a controversial issue in literature[17,18], was not prescribed to any of the studied patients.

We also observed that diuretics, especially the loop ones (furosemide), are still quite often prescribe; these are drugs have apparently fallen out of favor after they failed to demonstrate improvement in survival, but they are still prescribed to patients who present more advanced functional classes (NYHA FC III or IV)[19]. The third class of medications that influence survival are the aldosterone antagonists, specifically spironolactone[20]. Although only 53.1% of the studied population used the drug, 66.6% of the patients with an indication for its use (FC II or IV) were receiving it.

During the review of patients' evolution through the reading of the consultation description at the medical files, it was observed that there was a concern regarding the prescription of progressively higher doses of medications, which undoubtedly improved the clinical results[21]. The mean doses of ACEI, ARB and beta blockers prescribed were, at the moment of the consultation, respectively: 69.1%, 61.6% and 68.4% of the recommended dose. These figures show the need and the possibility of optimizing the treatment at the moment of the consultation. This is a concern to be kept in mind when the patient's clinical and hemodynamic conditions are favorable to such optimization.

The use of the prescribed medications is greatly due to the possibility that the patients would receive the medications for free after each consultation, and monthly, until the patient returns to the outpatient clinic. These medications are supplied by the Secretary of Health of the State of São Paulo. Also relevant is the fact that our outpatient clinic is part of a Heart Failure Clinic. This includes the participation of a multidisciplinary team, which consists of a nurse, social worker, psychologist, physical therapist, nutritionist, physical educator and dentist, who follow the patients periodically and promote disease awareness. The results are an increase in therapeutic adherence and reduction of the hospital admission rates[13].

The percentage of patients with comorbidities that are closely related to cardiovascular diseases (diabetes mellitus,

dyslipidemia and chronic renal failure) was another significant factor. The advance in the treatment of these diseases has allowed the patients' longer survival, making them more complex and instituting the polypharmacy among them.

The most important laboratory results were exactly the fasting glycemia that was above the recommended range and serum uric acid, which was also elevated. The use of diuretics can be considered one of the factors responsible for these findings.

Study limitations - Considering that the present study was a transversal analysis, it was not possible to analyze clinical outcomes related to the patients' treatment. Thus, this population will continue to be followed in order to allow the study of its clinical evolution.

Conclusion

After all the advancements reached in the last years, HF has shown to be a disease that requires knowledge and meticulous treatment optimization and patient management from the physician. The appearance of clinical units, with multidisciplinary teams specialized in the treatment of this disease has resulted in differentiated adherence rates and relevant clinical outcomes.

When aiming at studying how the patients from an outpatient clinic specialized in HF are being treated, the present study was able to demonstrate that such patients receive a medical prescription that is quite close to that recommended by the directives, with mean doses of medications that are also similar to that used in large studies.

These data reinforce the need of increasing the number of units specialized in HF, such as ours, either using the model adopted by InCor or having at least support from the nursing staff, which has also shown satisfactory results such as the decrease in the number of non-programmed hospital admissions, increased event-free time and reduced hospital costs[22].

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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