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Management of Chronic Heart Failure with Reduced Ejection Fraction in a Cameroonian Urban Setting: A Cross-Sectional Study

Prise en charge de l'insuffisance cardiaque chronique à fraction d'éjection réduite en milieu urbain camerounais : Étude observationnelle

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ABSTRACT

Purpose. To describe the current treatment of chronic heart failure with reduced ejection fraction in a self-selected population of Cameroonian patients and compare it with the recommendations of the European Society of Cardiology 2016 (ESC 2016). **Materials and Methods.** In a cross-sectional study, we included subjects with chronic heart failure with reduced ejection fraction from December 2018 to May 2018 in four hospital settings in Yaoundé, Cameroon. For each study participant, we collected clinical and para-clinical data related to drug and non-drug treatment. All these, through questioning and using the medical records of patients seen in an outpatient cardiology consultation. **Results.** A total of 87 patients, including 46 women and 41 men, participated in the study, with a mean age of 63.97 ± 13 years. The ejection fraction of our subjects ranged from 16 - 39%. 57% of the patients were on Angiotensin-converting enzyme inhibitors (ACEI), 22% on Angiotensin II receptor blockers (ARAII), 68% on beta-blockers, and 26% on potassium-sparing diuretics, 87% on loop diuretics, 11% on thiazide diuretics and 24% on digoxin. 59.77% were under the double combination ACEI and beta-blockers, 12.64% under triple combination ACEI, beta-blockers and diuretics. The maximum ESC 2016 recommended dose was reached in 4% of patients on ACEI, 3.38% on beta-blockers, 26.08% on potassium-sparing diuretics, 84.21% on loop diuretics and 100% on thiazide diuretics. 3.44% were taking contraindicated drugs such as non-steroidal anti-inflammatory drugs (NSAIDs). Patients consuming more than 5g/day of salt was found in 29% of patients, alcohol consumption in 29%, and tobacco consumption in 7%. **Conclusion.** The treatment of chronic heart failure with reduced ejection fraction is suboptimal in Cameroon. Based on these findings, there is a need for courses for health personal involved in managing these patients to regularly update and, above all, promote therapeutic education for these patients.

RÉSUMÉ

Objectif. Décrire le traitement de l'insuffisance cardiaque chronique à fraction d'éjection réduite dans une population de patients camerounais et le comparer aux recommandations de la Société Européenne de Cardiologie 2016 (ESC 2016). **Matériel et méthodes.** Dans une étude transversale, nous avons inclus des sujets atteints d'insuffisance cardiaque chronique avec fraction d'éjection réduite de décembre 2018 à mai 2018 dans quatre établissements hospitaliers de Yaoundé, au Cameroun. Pour chaque sujet, nous avons collecté des données cliniques et paracliniques liées au traitement médicamenteux et non médicamenteux. **Résultats.** Sur un total de 87 patients, 46 femmes et 41 hommes, avaient un âge moyen de 63,97±13 ans. La fraction d'éjection de nos sujets variait de 16 à 39%. 57% des patients étaient sous inhibiteurs de l'enzyme de conversion de l'angiotensine (IEC), 22% sous antagonistes des récepteurs de l'angiotensine II (ARAII), 68% sous bêtabloquants et 26% sous diurétiques d'épargne potassique, 87% sous diurétiques de l'anse, 11% sous diurétiques thiazidiques et 24% sous digoxine. 59,77% étaient sous la double association IEC-bêtabloquants, 12,64 % sous la triple association IEC-bêtabloquants-diurétiques. La dose maximale recommandée par l'ESC 2016 a été atteinte chez 4% des patients sous IEC, 3,38% sous bêtabloquants, 26,08% sous diurétiques épargneurs de potassium, 84,21% sous diurétiques de l'anse et 100 % sous diurétiques thiazidiques. 3,44% prenaient des médicaments contre-indiqués tels que les anti-inflammatoires non stéroïdiens (AINS). Des patients consommant plus de 5 g/jour de sel ont été retrouvés dans 29 % des cas, une consommation d'alcool chez 29% et une consommation de tabac chez 7%. **Conclusion.** Le traitement de l'insuffisance cardiaque chronique avec fraction d'éjection réduite est sous-optimal au Cameroun. Il existe un besoin en formations continues des personnels de santé impliqués dans la prise en charge de ces patients en plus de favoriser l'éducation thérapeutique de ces patients.

INTRODUCTION

The European Society of Cardiology 2016 (ESC 2016) defines heart failure as a clinical syndrome characterized by three elements: typical symptoms of heart failure (dyspnea at rest or on physical exertion, intolerance to physical exertion, oedema lower limbs); physical signs of heart failure (tachycardia, tachypnea, hepato-jugular reflux, lung crackles, pleural effusion, increased central venous pressure, peripheral oedema, hepatomegaly), objective evidence of a structural or functional abnormality of the heart at rest (cardiomegaly, a third heart sound, heart murmurs, abnormality noted on ultrasound, the elevation of natriuretic peptides) [1]. Heart failure is a significant public health problem. According to the ESC 2016 recommendations [1], its prevalence is approximately 1-2% of the adult population in developed countries and increases to over 10% in the population over 70 years of age. It is a public health issue and a significant economic issue due to the cost generated by its treatment, which is extremely high. This cost is estimated at 2% of all health expenditure in Western countries; in France, nearly one billion euros per year represents 1.5 to 2% of health expenditure, and 78% is related to hospitalization [2]. In Africa, despite the scarcity of work on heart failure (HF), it is considered the major complication of hypertension and the leading cause of admission to cardiology units, especially in patients with chronic hypertension.

In Cameroon, HF is a significant public health problem due to its high hospital prevalence (30%) and its overall mortality of 9.3% [3]. The ESC 2016 recommendations for managing chronic HF (CHF) are established and regularly updated. They highlight the beneficial effects of Angiotensin-converting enzyme inhibitors (ACEI), beta-blockers, and aldosterone antagonists based on extensive clinical trials. Numerous studies in Europe and the USA (Improvement study, Euro Heart Failure Survey study) have shown that the reference molecules in HF were insufficiently prescribed, making its treatment often sub-optimal with a lack of use of modern drug therapies and/or their prescription at too low a dose. To improve the treatment of chronic heart failure, particularly with reduced ejection fraction, we set out to describe this treatment in the Cameroonian hospital setting and compare the data in light of the current recommendations of the ESC 2016.

MATERIAL AND METHODS

Study design, settings, and participants

We carried out a descriptive cross-sectional study spanning from December 2017 to May 2018 (6 months) in three tertiary care (Yaoundé general hospital, Yaoundé central hospital and Yaoundé Teaching hospital) and one-second care hospital (Biyem-Assi district hospital) in Yaoundé, Cameroon. All these four health structures have cardiologists consultants and taking care of the heart's pathologies. Using consecutive convenience sampling, we recruited all consenting patients with chronic heart failure with reduced ejection fraction followed in those hospitals in the city of Yaoundé mentioned above. Excluded were those with acute heart failure or a preserved or intermediate ejection fraction.

The data collection for our research was done by questioning the patient's follow-up hospital files.

Studied variables

Using an established and pre-tested structured questionnaire, we studied socio-demographic data (age, sex, place of residence, marital status, level of education, profession), data relating to heart failure (discovery period, findings on ECG and echocardiography specifying the ejection fraction, the aetiology of the heart failure, the severity of the heart failure according to the NYHA classification), data relating to the patient's follow-up (the attending health personnel such as the cardiologist, general practitioner, nurse and others, the follow-up health structure, the frequency of consultation of the attending physician), drug treatment (therapeutic class and current dose), non-drug treatment (diet by specifying the cumulative amount of salt that the patient ingests per day, the consumption of alcohol, tobacco and/or contraindicated drug consumption), comorbidities and the means of their management.

Definitions of operational terms

Reduced heart failure fraction is defined as a left ventricular ejection fraction (LVEF) <40% [1].

Statistical analysis

The data were recorded analyzed using SPSS 20, Excell 2013 and cspro7.0 software.

Ethical considerations

Ethics clearance was obtained from the Institutional Review Board of the University of the Montagnes of Bangangte in Cameroon (Authorization No. 2018/203 / UdM / PR / CIE), followed by obtaining research authorizations from the directorate of each study hospital. The study was carried out following the fundamental principles of medical research of the Declaration of Helsinki [4] and good clinical practice codes.

RESULTS

General characteristics of participants

We enrolled 87 patients in the study. The female sex was the most represented (53%). Our population's mean age was 63.97 ± 13 years (range varying between 26 and 90 years). The most designated age group was 60-69 years old. The majority of patients in our study had primary education or less (62%). Almost half of the patients (55.17%) did not have a monthly income. NYHA Stage III patients were the most represented (45%). Concerning the comorbidities, hypertension was the most frequent (58%), followed by Type 2 diabetes (14%). HF patients were treated with the following drug classes: ACEI, Angiotensin II receptor blockers (ARA II), beta-blockers, diuretics, and calcium channel blockers. Among the type 2 diabetics, 92% (n = 11) used oral anti-diabetic drugs (OAD). The main drug prescribed was metformin followed by gliclazide which was prescribed only in combination with metformin in two patients; 8% were on insulin. Concerning aetiologies of HF, hypertension and dilated cardiomyopathies were the most frequent (38.18%, each one). See Table I.

Tableau I : General characteristics of the study population

Variables	Categories	n	%
Age	Less than 40 years	5	5.75
	40 – 49 years	5	5.75
	50 – 59 years	16	18.39
	60 – 69 years	31	35.63
	70 – 79 years	26	29.89
	More than 79 years	4	4.6
Gender	Male	41	47
	Female	46	53
Level of education	Not formal	16	18
	Primary	38	44
	Secondary	23	26
	Tertiary	10	12
Employment status	Employed	39	44.83
	Unemployed	48	55.17
NYHA Stage	II	37	42
	III	39	45
	IV	11	13
Comorbidities	Hypertension	51	58
	Diabetes	12	14
	Stroke	6	7
	Anemia	6	7
	Gout	5	5
	Renal failure	5	5
	obesity	2	1
The different types of treatment for certain comorbidities of heart failure	Hypertension	ACEI, ARB II, beta-blockers, diuretics et Calcium channel blokers.	
	Diabetes	Metformine alone, glicazide plus metformine and insuline seul	
	Stroke	ACEI, ARB II, beta-blockers, diuretics and Calcium channel blokers, aspirine, statins depending on the type of stroke and the presence of dyslipidemia<	
	Anemia	Iron and folic acid	
	Gout	allopurinol and febuxoxtat.	
Etiology of Chronic heart failure	Dilated cardiomyopathy	28	32.18
	Hypertensive cardiopathy	28	32.18
	Valvular heart disease	14	16.1
	Ischemic heart disease	12	13.8
	Toxic cardiopathy	2	2.3
	Congenital cardiopathy	2	2.3
	Arrhythmia	1	1.16
The mean left ventricular ejection fraction	16 - 39% ± 8.54 %.		

ACEI: Angiotesin converting enzyme inhibitors, ARB II: Angiotesin II receptor blokers

Therapeutic classes and associations

Loop diuretics were the most widely prescribed therapeutic class. The combination ACEI and beta-blocker were found in 59.77% of patients, while the triple combination of ACEI, Beta-blockers and diuretics was prescribed in 12.64% of patients. Ramipril and Perindopril were the most prescribed ACEI (46% for each). Enalapril and Lisinopril (2% each) were prescribed less frequently. Losartan was the most prescribed ARA II (84.21%). Irbesartan was prescribed less (5.26%). Nebivolol was the most prescribed beta-blocker. Furosemide was the most prescribed loop diuretic (89.47%). Hydrochlorothiazide was prescribed in 90% in its drug class, followed by Altizide in 10%. Of the 19 patients with atrial fibrillation, 15 were on anticoagulants (78.94%). Acenocoumarol was the most prescribed anticoagulant (Table II). We found a rate of treatment with contraindicated molecules such as non-steroidal anti-inflammatory drugs (NSAIDs) of 3.44% (n = 3), in particular Ketoprofen (33.33%), Aceclofenac (33. 3%) and Eterocoxib in 33.33% of cases. Consumption of salt over 5g per day was found in 29% of patients, including alcohol abuse (29%) and tobacco abuse in 7% of patients.

Tableau II:Treatment of chronic heart failure with reduced ventricular ejection fraction

Variables	Categories	n	%
Therapeutic classes used for the treatment of heart failure	Loop diuretics	76	87
	Potassium sparing diuretics	23	26
	Thiazidide diuretics	10	11
	Beta-blokers	59	68
	ACEI	50	57
	Digoxin	21	24
	ARA II	19	22
The prescription rate of ACEI	Ramipril	23	46
	Pendopril	23	46
	Captopril	2	4
	Enalapril	1	2
	Lisinopril	1	2
The prescription rate of ARA II	Lorsatan	16	84
	Candesartan	2	11
	Irbesartan	1	5
	Valsartan	0	0
The prescription rate of beta-blokers	Nebivolol	31	53
	Bisoprolol	23	39
	Atenolol	3	5
	Carvedilol	2	3
The prescription rate of loop diuretics	Furosemide	68	89
	Bumetadine	5	7
	Torasemide	3	4
The prescription rate of thiazide diuretics	Hydrchlorothiazide	9	90
	Altizide	1	10
The rate of prescription of anticoagulants in patients with atrial fibrillation	Acenocoumarol	11	73.33
	Fluidione	2	13.33
	Rivaroxaban	2	13.33
The rate of prescription of contraindicated drugs such as non-steroidal anti-inflammatory drugs	Ketoprofene	29	33.33
	Aciclofenac	29	33.33
	Eterocoxib	29	33.33
The rate of prescription of life style modification measures	Alcohol consumption	25	29
	Salt consumption ≤ 5g/day	62	71
	Salt consumption > 5g/day	25	29
	Tobacco consumption	6	7

ACEI: Angiotesin converting enzyme inhibitors, ARA II: Angiotesin II receptor blokers

Recommended doses

Only thiazide diuretics were prescribed at the recommended doses. More than half of the patients on loop diuretics (84.21%) had reached the maximum recommended dose. The therapeutic classes that were prescribed at low doses were ACEI, beta-blockers, ARBs II and aldosterone antagonists (Table III).

Tableau III : 2016 ESC guideline recommended doses in every drug class

Drug class	Total Number of patients on this drug	Total number of patients on 2016 ESC recommended maximal doses	Percentage patients on 2016 ESC recommended maximal doses (%)
ACEI	50	2	4
Beta-blokers	59	2	3.38
ARA II	19	0	0
Potassium sparing Diuretics	23	6	26.08
Loop Diuretics	76	64	84.21
Thiazide Diuretics	10	10	100

ACEI: Angiotesin converting enzyme inhibitors, ARA II: Angiotesin II receptor blokers

DISCUSSION

This study aimed to describe the current treatment of chronic heart failure (CHF) with reduced ejection fraction in a group of Cameroonian patients and compare it with the recommendations of the European Society of Cardiology 2016 to be able to deduce the quality of care delivered to patients with CHF with reduced ejection fraction in Cameroon. Through a multicenter cross-sectional study in four centres of cardiologist consultation in Yaoundé, Cameroon. Our findings are as follows the mean ejection fraction varied from 16% to 39%. 57% of the patients were on ACEI, 22% on ARA II, 68% on beta-blockers, 26% on potassium-sparing diuretics, 87% on loop diuretics, 11% on thiazide diuretics and 24% on digoxin. 59.77% were under the double combination ACEI and beta-blockers, 12.64% under triple combination ACEI, beta-blockers and diuretics. The maximum recommended dose was reached in 4% of patients on ACEI, 3.38% on beta-blockers, 26.08% on potassium-sparing diuretics, 84.21% on loop diuretics and 100% on thiazide diuretics.

ACEI has been shown to reduce mortality and morbidity in HF patients with reduced ejection fraction [5]. They are, therefore, recommended in all symptomatic HF patients who do not have any contraindication (bilateral renal artery stenosis, history of angioedema during exposure to ACE inhibitors) [1]. Our study found insufficient prescription of this therapeutic class at 57% among patients. This poor prescription could be explained by the intolerance of the adverse effects noted in some patients (in this case, they were prescribed ARA II), the low socioeconomic level of some patients (55.17% without monthly income) not allowing them to obtain all the specified molecules. Beta-blockers, long contraindicated, have been shown in recent years to be an effective treatment for HF [6]. They reduce mortality and morbidity in symptomatic patients with reduced ejection fraction despite therapy with ACEI and, in most cases, a diuretic [1]. Among the 32% who did not receive this therapeutic class, some had contraindications, including chronic obstructive pulmonary diseases (COPD) (1.15%), atrioventricular blocks (AVB). The ESC 2016 guidelines recommend this therapeutic class at the time of

diagnosis combined with an ACEI and in the absence of contraindication. We can, therefore, conclude here that the recommendations have been respected.

ESC 2016 published several controlled studies with a placebo group, including that of Packer et al. in 2001, which demonstrated that the combination of a beta-blocker with an ACEI and a diuretic decreases patients' mortality suffering from heart failure. This triple association was found in only 12.64% of patients. This insufficient prescription could be explained by the absence and/or low monthly income of some patients, which does not allow them to obtain all the prescribed drugs. Also, contraindications to certain drugs (COPD and AVB for beta-blockers) are noted as a factor limiting this triple association. Diuretics are recommended to reduce signs of congestion in patients with HF with reduced ejection fraction, but their effects on mortality have not been studied in randomized controlled trials. A systematic review with meta-analysis showed that in patients with CHF, loop diuretics, and thiazides reduced the risk of death, worsening HF and improved physical exercise capacity compared to placebo and diuretics [1]. In our study, this therapeutic class was widely used, particularly loop diuretics (87%) with the profile of thiazide diuretics and aldosterone antagonists.

Their speed of action could explain this predominance of prescription loop diuretics compared to other diuretics. However, ESC 2016 recommends the use of diuretics during congestive periods of HF [1]. We found long-term use of this therapeutic class even outside of congestive states in some patients, which does not meet the ESC 2016 recommendations. Ouyang et al. [8] and the carried out in 2015 show that digoxin in patients with reduced ejection fraction and atrial fibrillation is still controversial. According to Ouyang et al. [8] and the ESC 2016 guidelines [1], its use would potentially increase mortality and hospitalizations. On the other hand, the meta-analysis reported by Ziff et al. found that the use of digoxin in patients with these criteria has no harmful effect on mortality [1]. In our study, it was prescribed in 24% of patients.

Our study found that ACEI, ARA II, beta-blockers, and aldosterone antagonists (spironolactone) were prescribed at shallow doses. Only 4% of patients reached the maximum recommended dose for ACEI, 3.38% for beta-blockers, and 26.08% for aldosterone antagonists. None of the patients using ARA II got the recommended dose. This leads us to conclude that these drugs used are prescribed at low doses, making our patients sub-optimal. These results are similar to the study conducted by Maggioni et al. in 2013, which found evidence that in clinical practice, the majority of patients receive sub-optimal doses of prescribed drugs, including ACEI [7]. This could be explained by the non-respect of follow-up appointments on the part of the patients, or the titration of the doses of the drug used is made by the cardiologists.

Nevertheless, treatment was optimal for loop diuretics and thiazides as more than half (84.21%) of patients using loop diuretics had reached the recommended dose. All those using thiazides had met the dose recommended. This could be justified by the frequency of handling this therapeutic class (the most prescribed class in the patients in this study) and the prescription from the initiation of a high dose to relieve the patient of congestive symptoms on admission. About 4% (n = 3) of patients were taking drugs that were contraindicated in treating heart failure, including NSAIDs such as Ketoprofen, Aceclofenac and Eterocoxib. These drugs were prescribed to treat lumbar osteoarthritis. The ESC 2016, via the work of Eschenhagen et al. in 2011, reports that NSAIDs given to treat comorbidities such as rheumatological pathologies worsens the course of heart failure [1]. Our results do not meet the recommendations, although they are prescribed in a small population. Regarding lifestyle modification measures, in particular salt consumption > 5g/day (71%), alcohol consumption (29%) and tobacco consumption (7%) were not respected in some patients. These results could be explained by the low level of education of the patients (level of education which allows them to understand the interest of the different modalities of their treatment) on the one hand and the absence of counselling in some of them by their cardiologists on the other hand.

Our study's limitations are its small sample size (n = 87), making our results generalized with caution. Also, the therapeutic compliance of drugs for CHF and their dosages prescribed by the treating staff for patients treated for HF were assessed subjectively in patients. So it is possible that we had the inclusion of a selection bias in our study. However, this study is one of the first to describe the management of subjects with CHF with a reduced ejection fraction in conformity to an international norm (ESC 2016) in sub-Saharan Africa geared at improving the health care, follow-up and quality of life of CHF with a reduced ejection fraction in Cameroon.

CONCLUSION

The study findings suggest that compared to international standards such as those of the European Society of Cardiology 2016, the treatment of chronic heart failure with reduced ejection fraction in Cameroon remains sub-optimal. From a therapeutic point of view, to improve the management of these patients, it is necessary to optimize the prescription and dosages of ACEI, beta-blockers, diuretics, ARA II, and anti-aldosterones have been prescribed either insufficiently or at low doses. It is necessary to stop prescription drugs not recommended, such as altizide, atenolol, and NSAIDs used in Cameroon. Also, the health providers of HF patients must reinforce the use of the lifestyle modification measures not used by the majority of our partners. Finally, it is important to avoid prescribing the long-term use of diuretics in the absence of congestive signs as these drugs are not without side effects nor free of charge for a population which is mainly unemployed.

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