Research in Social and Administrative Pharmacy xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

Adherence to the evidence-based heart failure drug treatment: Are there sex-specific differences among new users?

J.F. Kayibanda[a,b,d,*], C. Girouard[a,b,c], J.-P. Grégoire[a,b,c], E. Demers[b,c], J. Moisan[a,b,c]

[a] Faculty of Pharmacy, Université Laval, Québec, QC, Canada
[b] Chair on Adherence to Treatments, Université Laval, Québec, QC, Canada
[c] Axe Santé des Populations et Pratiques Optimales en Santé, Centre de Recherche du CHU de Québec, Université Laval, Québec, QC, Canada
[d] Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, United States of America

ARTICLE INFO

Keywords:
Heart failure
Sex-based differences
Persistence or compliance
New users
Evidence based drug treatment

ABSTRACT

Background: The evidence-based heart failure (HF) drug treatment is made of a β-blocker and an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker, or hydralazine + isosorbide dinitrate. Little is known about sex-based difference in adherence to the evidence-based HF drug treatment.
Objectives: To assess among new users of the evidence-based HF drug treatment, the association between sex and 1) persistence with the treatment 1 year after its initiation, 2) implementation of the treatment among those who persisted, and 3) overall adherence to treatment in the year following its initiation. *Methods:* A cohort study was conducted among new users of this treatment using Quebec medico-administrative data. Patients still on the evidence-based HF drug treatment one year after initiation were considered persistent. Among persistent users, those with ≥88% of days covered by the treatment were deemed to have adequately implemented it. Persistent patients who have adequately implemented the treatment were considered adherent. To measure the association between, on one hand sex, and on the other persistence, implementation and adherence, adjusted proportion ratios (APR) with their 95% confidence intervals (CI) were calculated.
Results: Among 13,453 women, 72.1% were persistent, 72.2% adequately implemented the treatment, and 52.8% were adherent. Among the 14,614 men, these proportions were 73.6%, 67.9% and 50.1%, respectively. Men were less likely than women to be adherent to their treatment (APR: 0.96, 95% CI: 0.94–0.99).
Conclusion: Among individuals initiating an evidence-based multi-drug treatment for HF, men are less likely than women to be adherent to this treatment.

1. Introduction

Heart failure (HF) is a chronic disorder associated with high mortality and morbidity. It is estimated that 26 million people have HF worldwide.[1] More than 40,000 Canadians died with HF between 2000 and 2009 representing 2% of all deaths.[2] In 2010, the cost of HF in the United States of America was estimated at $24.7 billion and was projected to increase to $77.7 billion by 2030.[1] In Canada, the mean hospitalization cost incurred by HF patients during their last six months of life was Can$26,186 in 2006.[3]

According to some clinical guidelines,[4–6] a combination of carvedilol metoprolol or bisoprolol, (we refer to them as β-blockers) and an angiotensin-converting enzyme inhibitor (ACEi) should be prescribed to all patients diagnosed with HF to reduce the risks of morbidity and mortality associated with HF. If an ACEi is not tolerated, an angiotensin receptor blocker (ARB) can be used. The combination of isosorbide dinitrate and hydralazine may be considered for HF patients who do not tolerate ACEis and ARBs. Thus, the evidence-based HF drug treatment should be made of a combination of a β-blockerand either an ACEi, an ARB, or hydralazine plus isosorbide dinitrate.

However, to benefit from their treatment, patients have to adhere to it, i.e. to take their medication as prescribed.[7] Adherence to drug treatment is made of three components: initiation, persistence and implementation.[7,8] Patients who have initiated a drug treatment are persistent if they take it for the recommended duration. Even if they persist with their treatment, patients also need to implement it adequately, i.e. to take the drug treatment as recommended in terms of dosing regimen. It has been observed that a poor adherence to HF drug treatment is associated with an increased number of emergency department visits,[9,10] hospitalizations[9,11] and deaths (all causes mortality).[11–13]

Sex-related differences have been reported in many aspects of HF

* Corresponding author.
E-mail address: jfkayibanda@nursph.org (J.F. Kayibanda).

http://dx.doi.org/10.1016/j.sapharm.2017.10.010
Received 4 April 2017; Received in revised form 24 October 2017; Accepted 24 October 2017

disease.[14] For example, the age-adjusted HF incidence rates were found to be higher among men than women,[15,16] women were significantly less to experience a cardiovascular admission,[17] to receive implantable cardioverter-defibrillators therapy[18,19] but have better survival than men.[17,20,21]

In regard to adherence to the evidence-based HF drug treatment, to the best of our knowledge, it has never been compared between men and women. Moreover, the two underlying adherence components (persistence and implementation) have never been assessed in the same study.

The objectives of this study were to assess in new users of evidence-based HF drug treatment, the association between sex and1) persistence with the evidence-based HF drug treatment 1 year after its initiation, 2) implementation of the evidence-based HF drug treatment among those who persisted and 3) adherence (i.e. both persistence and adequate implementation) to the evidence-based HF drug treatment in the year following its initiation.

2. Methods

2.1. Study design and data sources

A n inception cohort study of new users of evidence-based HF drug treatment was conducted using data administered by the Quebec Health Insurance Board (*Régie de l'assurance maladie du Québec, (RAMQ)*), and the Quebec Institute of Statistics. Quebec permanent residents are all covered by RAMQ for medical services and hospitalizations. The RAMQ public drug plan covers over 94% of residents aged ≥65 years, welfare recipients and all persons who are not covered by a private drug insurance group plan for a total of 3.3 million individuals insured in 2011.[22] In addition to data on individuals (age, sex, guaranteed income supplement recipient, and area of residence) and prescribed drugs dispensed (drug identity, dispensing date, number of days' supply and prescriber specialty), RAMQ administrative data include information on ambulatory health services (date, specialty of the physician consulted, main diagnosis) and hospitalizations (admission date, main and secondary diagnoses, and duration of stay). Finally, RAMQ data can be linked to vital statistic information obtained from the Quebec Institute of Statistics.

2.2. Study population

The source population consisted of all RAMQ beneficiaries aged ≥18 years with at least one HF diagnosis (ICD-9 codes: 428, ICD-10 codes: i50) between January 1, 2000 and December 31, 2009, inclusively. From this source population, RAMQ eliminated individuals who had not been constantly eligible for the public drug plan in the year prior to the first recorded HF diagnosis. This minimum look-back period allowed to make sure the first recorded HF diagnosis was indeed the first one. RAMQ sent data recorded for those individuals until December 31, 2009, death or end of eligibility to the drug plan.

Using data received from RAMQ, individuals with only one HF diagnosis were then excluded unless this diagnosis was inpatient. If the initial HF diagnosis was outpatient, individuals were included if there was a second HF diagnosis (either outpatient or inpatient) within one year. Schultz et al. has shown this procedure to be valid at identifying HF cases using administrative data.[23] If there was more than one HF diagnosis, the date of the first recorded one was considered the date at which HF was diagnosed.

The study population was further restricted to new users of the evidence based HF drug treatment between the date of HF diagnosis up to December 31, 2009, loss of eligibility to the drug plan or death, whichever came first. Users of the evidence based HF drug treatment were defined as those who had concomitant claims for, on one hand, a β-blocker (carvedilol, metoprolol or bisoprolol) and, on the other hand, an ACEi (captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, trandolapril) or an ARB (candesartan, valsartan, eprosartan, irbesartan, losartan, telmisartan, olmesartan), or hydralazine plus isosorbide dinitrate. Those exposed to the evidence based HF drug treatment in the 365-day period prior to and including the date of HF diagnosis, were excluded. Finally, in order to assess persistence with and implementation of the evidence-based HF drug treatment over a 1-year period, those who did not have a follow-up of at least 365 days starting at the date of initiation of the evidence-based HF drug treatment were also excluded. It is noteworthy that continuous drug plan coverage was needed for three periods: the 365-day period preceding the HF diagnosis, and the 365-day period preceding and the 365-day period following the evidence-based HF drug treatment initiation.

Data acquisition was authorized by the *Commission d'accès à l'information du Québec* and the study was approved by the CHU de Québec ethics Committee.

2.3. Variables

Three dependant variables were measured in the 365 days after

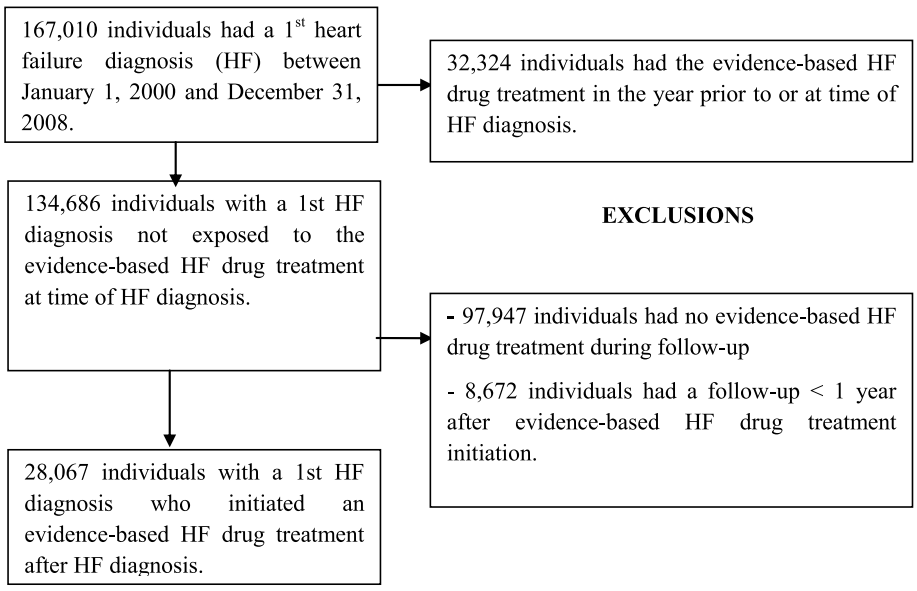

Fig. 1. Selection of the study population.