Negative Clinical Outcomes Associated With Drug-Related Problems in Heart Failure (HF) Outpatients: Impact of a Pharmacist in a Multidisciplinary HF Clinic

PALOMA GASTELURRUTIA, MS,[1,2] SHALOM ISAAC BENRIMOJ, PhD, BPharm,[3] JOSÉ ESPEJO, PharmD, PhD,[4] LAURA TUNEU, PharmD, PhD,[2,4] M. ANTONIA MANGUES, PharmD, PhD,[2] AND ANTONI BAYES-GENIS, MD, PhD, FESC[1,5]

Badalona, Barcelona, and Granada, Spain; and Sydney, Australia

ABSTRACT

Background: Drug-related negative outcomes (DNOs) are health problems that patients experience due to drug use or nonuse. Heart failure (HF) patients are at high risk of experiencing DNOs owing to polypharmacy, comorbidities, and age.

Methods and Results: Ninety-seven consecutive HF patients were enrolled and followed for 6 months. A pharmacist, integrated within a multidisciplinary HF team, reviewed the medication of each patient to detect, resolve, and/or prevent possible DNOs, risks of developing a DNO (rDNOs) and the drug-related problems (DRPs) that are associated with them. We detected 147 DNOs/rDNOs with a mean of 1.5 ± 1.4 per patient. Among DNOs, 45% were due to a lack of a pharmacologic treatment (need for a drug) and 24% were treatments with an insufficient drug dose (quantitative ineffectiveness). Among rDNOs, 33% were due to use of an unsafe drug (nonquantitative lack of safety) and 30% to quantitative ineffectiveness. Ninety-four percent of DNOs/rDNOs were preventable, and, importantly, 5.5% were classified as clinically serious. During follow-up, pharmacist interventions solved or prevented the health problem in 83% of cases. The most frequently identified DRPs were "insufficiently treated health problem" (31%), "inadequate dose, regimen, or duration of a drug" (22%), "probability of adverse effects" (16%), and "nonadherence" (14%). A significant relationship between the number of DNOs/rDNOs and the number of drugs was found ($P < .013$).

Conclusions: Chronic HF outpatients have a high incidence of preventable DNOs. The inclusion of a pharmacist in multidisciplinary HF teams should be considered, because it is clinically beneficial for patients and it increases HF specialists' awareness of DNOs, especially those beyond HF. (*J Cardiac Fail 2011;17:217–223*)

Key Words: Heart failure, drug-related problems, drug-related negative outcomes, pharmaceutical care.

In Western countries the number of heart failure (HF) patients is rising, mainly owing to the aging of the population and the increase in survival among coronary disease and hypertensive patients.[1] In spite of effective pharmacologic treatments, HF remains a debilitating disease for both the patient and the associated health care system,[2] because HF patients exhibit high morbidity and mortality.[3] Multidisciplinary HF management units have been developed and have shown to reduce the number of hospital readmissions, number of days in hospital, and the cost of care, with a parallel increase in patient quality of life and survival rate.[2,4,5]

There is strong evidence that morbidity related to medicines is a major health issue; Howard et al examined hospital admissions in a cohort of 4,093 patients and found that 6.5% of admissions were judged to be drug related, with 67% of them judged to be preventable.[6] Baena et al reported that 33.3% of emergency department visits were caused by drug-related negative outcomes (DNOs), 73% of which were preventable, with an average cost per

From the [1]Cardiology Service, Hospital Universitari Germans Trias i Pujol, Badalona, Spain; [2]Pharmacy Service, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [3]Faculty of Pharmacy, University of Sydney, Sydney, Australia; [4]Pharmaceutical Care Research Group, University of Granada, Granada, Spain and [5]Department of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain.

Manuscript received June 15, 2010; revised manuscript received September 16, 2010; revised manuscript accepted October 25, 2010.

Reprint requests: Antoni Bayes-Genis, MD, PhD, FESC, Chair, Cardiology Service, Hospital Universitari Germans Trias i Pujol, Carretera de Canyet s/n 08912, Badalona (Barcelona), Spain. Tel: +34 934978915. Fax: +34 934978939. E-mail: abayesgenis@gmail.com

See page 222 for disclosure information.

1071-9164/$ - see front matter

doi:10.1016/j.cardfail.2010.10.009

DNO of 329.5 Euros (~426 US dollars).[7] Blix et al identified a DNO in 81% of 827 inpatients, with a median of 2.1 clinically relevant DNOs per patient.[8] As a population, HF patients have advanced age, several comorbidities, and polymedication leading to problems through drug interactions, adverse effects, and/or poor adherence to the prescribed drug regimen.[9,10]

The inclusion of a pharmacist in a multidisciplinary team has been shown to be beneficial. HF patients who were included in a pharmaceutical care program improved in clinical parameters such as exercise capacity and experienced fewer hospital readmissions.[9] Gattis et al observed that including a pharmacist as a member of a multidisciplinary HF team significantly reduced all-cause mortality and HF events.[11] A systematic review of randomized trials by Koshman et al concluded that pharmacist care in the treatment of patients with HF greatly reduces the risk of all-cause and HF hospitalizations.[12] And more recently, Roughead et al demonstrated that practitioner-pharmacist collaborative home medication review was effective in delaying the time to next hospitalization for HF.[13]

To our knowledge, no study has assessed the characteristics of HF DNOs and the efficacy of pharmacist intervention in their resolution. In the present study, we assessed the prevalence and characteristics of DNOs, the risks of developing a DNO (rDNOs), and the drug-related problems (DRPs) that are associated with them, documenting the results of pharmacist intervention in an HF outpatient cohort.

Methods

Study Population and Design

Consecutive patients were enrolled at the HF ambulatory clinic of a university hospital in Barcelona (Spain) between October 2008 and April 2009. All patients also visited their primary care physician regularly. The exclusion criterion was previous visit with the pharmacist at the HF clinic. Patient clinical status as well as biochemical and echocardiographic data were obtained upon patient enrollment. Patients were clinically followed for 6 months. A pharmacist, with a postgraduate master's degree in pharmaceutical care and with HF care clinical expertise, integrated in the multidisciplinary team reviewed the medicines taken by each patient, detecting DNOs and rDNOs associated with DRPs using the Dader method, a methodology for medication review with follow-up.[14] When a DNO/rDNO was detected, a pharmacist intervention was suggested to the patient if the DNO/rDNO was related to over-the-counter (OTC) drugs, adherence, drug administration, or nonpharmacologic measures or to the doctor in all other cases. Data were obtained from the clinical history and from patient interviews. This investigation conformed to the principles outlined in the Declaration of Helsinki, it was approved by the hospital Ethics Committee, and each of the patients signed an informed consent.

HF severity was assessed by the New York Heart Association (NYHA) criteria,[15] and an objective HF clinical disease severity score (CDSS) based on Framingham criteria was used to diagnose destabilized HF.[16,17]

Variable Definitions

DRPs are defined as "situations where the process of use of medication causes, or may cause, a negative clinical outcome"[14] (Table 1). The methodology used herein focused on clinical negative outcomes, so DRPs were considered only as a potential cause of DNOs/rDNOs.

DNOs associated with DRPs are defined as "health problems that appear due to the use or nonuse of medicines," and rDNOs are "situations where the patient is at risk of suffering a negative change in health status (a new health problem)."[18,19] DNOs/rDNOs are classified into 3 categories and 6 subcategories as shown in Table 1: 1) necessity: unneeded versus needed drugs; 2) effectiveness (eg, subdosage, drug interactions resulting in a lower effect); and 3) safety (eg, overdosage, drug interactions resulting in adverse effects, allergy, and/or contraindication). Further classification into quantitative and nonquantitative was made if the DRP in (2) and (3) was related to the dosage of the drug or not.[20]

A health problem is defined by the World Organization of Family Doctors (WONCA) as "any concern in relation to the health of a patient as determined by the patient and/or the health care provider."[21] We classified health problems according to the International Classification of Diseases, 10th edition.[22]

A pharmacist intervention, any measure with the goal of improving health or altering the course of disease,[23] was proposed when no action was taken from the rest of the health team. The result was assessed according to the criteria described by the Cipolle classification, (resolved, stable, improved, partial improvement, unimproved, worsened, failed, and expired),[24] and was modified to include 2 additional risk categories for assessing the result of a pharmacist intervention on a rDNO: "health problem prevention" when the rDNO was solved, and "risk persistence" when it was not). Severity was assessed by 3 HF doctors (2 cardiologists and 1 internal medicine specialist) on a 3-category scale (slight, moderate, serious) for adverse reactions; slight and

Table 1. Classification of Drug-Related Problems (DRPs), Drug-Related Negative Outcomes (DNOs) and Risks of a DNO (rDNOs)

DRPs	Erroneous administration of the drug
	Personal characteristics
	Inappropriate drug storage
	Contraindication
	Inappropriate dose, drug regimen, and/or duration
	Duplication
	Dispensing errors
	Prescription errors
	Nonadherence
	Interactions
	Other health problems that affect treatment
	Adverse effects probability
	Insufficiently treat health problem
	A nonneeded medicine is being taken
	Other
DNOs/rDNOs	The patient presents a health problem:
	(1) Necessity:
	1. that is not being treated.
	2. caused by an unnecessary drug.
	(2) Effectiveness:
	3. due to a nonquantitative ineffectiveness of a drug.
	4. due to a quantitative ineffectiveness of a drug.
	(3) Safety:
	5. due to a nonquantitative lack of safety of a drug.
	6. due to a quantitative lack of safety of a drug.

moderate were determined by clinical decision, and serious was defined as a problem causing death, threatening the patient's life, causing or prolonging hospitalization, causing significant or persistent disability or incapacity, or causing a congenital anomaly or birth defect.[25] Preventability was assessed by using the Schumock and Thorton[26] questionnaire modified by Baena et al.[27]

Statistical Methods

The sample size was calculated based on a preliminary analysis of a population from the same HF clinic in which 60% of patients had ≥1 DNO/rDNO. For a 10% precision estimation, to achieve a 95% asymptotic normal confidence interval, a minimum of 93 patients was required. Descriptive analyses were performed. Categoric variables were described by frequencies and percentages, and continuous variables were described by means and standard deviations. Medication reviews with follow-up variables were collected within the 6-month follow-up, and correlations were assessed by Pearson or Spearman tests according to normal or nonnormal distribution of variables. Statistical analyses were performed with SPSS v.17 (SPSS, Chicago, Illinois). A 2-sided P value of $<.05$ was considered to be statistically significant.

Results

Ninety-seven HF patients were enrolled in the present study, with a mean number of medicines used of 10.2 ± 3.2. The majority of patients were in New York Heart Association functional classes II (46%) and III (52%) at inclusion. Forty-five percent of patients had preserved systolic function versus 54.6% with systolic dysfunction. However, the 2 groups were similar with a mean number of medicines taken of 10 (10.1 for preserved vs 10.6 for depressed; P = NS), and similar treatment. Table 2 displays demographic, clinical, and biochemical data, as well as the treatment at enrollment. The number of pharmacist visits during the 6-month follow-up ranged from 1 to 11 (mean 3.5), depending on the patients' HF clinic visits according to clinical status.

We detected 147 DNOs/rDNOs; of these, 87 were a health problem and 60 were a risk of developing a health problem, with ≥1 DNO/rDNO in 78% of patients (n = 76). A mean of 1.5 DNOs/rDNOs per patient was found, with a maximum of 6 per patient during follow-up (Table 3). There were no significant differences between patients with systolic dysfunction or preserved systolic function in terms of number of DNOs/rDNOs (P = 0.37 and P = 0.24, respectively). When assessing the DNOs, we found that 45% of health problems were due to a lack of pharmacologic treatment (need of a drug), and 24% were treated with an insufficient drug dose (quantitative ineffectiveness). When assessing rDNOs, 33.5% were due to using a drug that was not safe in that patient (nonquantitative lack of safety) and 30% were due to quantitative ineffectiveness.

Twenty-two percent (n = 33) of the DNOs/rDNOs were due to HF medications (angiotensin-converting enzyme inhibitor/angiotensin-receptor blockers, beta-blockers, antialdosterone drugs, diuretics, potassium supplements, and digoxin). The drugs that were most frequently associated with DNOs were allopurinol (19%), diuretics (13%), and diabetes mellitus treatment drugs, including oral antidiabetics (OAD) and insulin (12%). The drugs involved with rDNOs were diuretics (15%), antiplatelet drugs (13%), and omeprazole (0.9%).

Table 2. Demographic, Clinical, Biochemical, and Treatment Data for the Studied Population (n = 97)

Variable	
Demographic	
Age, y	74.5 ± 9.6
Male, %	66
Clinical	
Ischemic etiology, %	40.2
Sinusal rhythm, %	46.3
NYHA functional class II/III, %	45.8/52.1
CDSS	1.85 ± 1.4
LVEF, %	44.6 ± 16.1
Diabetes, %	54.6
Dyslipidemia, %	58.8
Current smoker,%	10.3
Hypertension, %	85.6
Biochemical	
NT-proBNP, ng/L	4,891.3 ± 6,594.8
Hemoglobin, g/L	123.8 ± 22.8
eGFR, mL min^{-1} 1.73 m^{-2}	48.8 ± 14.5
Treatment	
No. of medicines	10.2 ± 3.2
Diuretics, %	95.9
ACEI/ARB, %	76.3
Beta-blockers, %	54.6
Digoxin, %	29.9
Amiodarone, %	13.4
Aldosterone antagonists, %	42.3
Statins, %	61.9
Anticoagulants, %	52.6
Antiplatelets, %	49.5
Proton pump inhibitors, %	78.4
Benzodiazepines, %	39.2
OAD/insulin, %	40.2
Allopurinol, %	23.7
Inhalers, %	34
Iron, %	19.6

NYHA, New York Heart Association; CDSS, clinical disease severity score; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro−B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers; OAD, oral antidiabetics.

The most frequent health problems detected were uncontrolled serum uric acid levels (ICD-10 R79, 18.5% of cases) and uncontrolled diabetes (ICD-10 E10−14, 12% of cases), followed by anemia and constipation (ICD-10 D50−64 and K59.0, respectively, 8.5% of cases). Gastric injury from antiplatelet drugs (ICD-10 Y44.2 and Y44.4) was the most frequent health problem (23% of cases) at risk of occurrence due to drug use (the patient having ≥2 of the following characteristics: >65 years old, concomitant nonsteroidal antiinflammatory drug or anticoagulant treatment, and gastrointestinal symptoms or history of gastrointestinal disease.[28]

The most frequent DRPs identified (Table 4) were "insufficiently treated health problem" (31%), "inappropriate dose, drug regimen, and/or duration" (22%), "adverse effects probability" (16%), and nonadherence (14%). The most prevalent DRP found when assessing diuretics was

Table 3. Drug-Related Negative Outcomes (DNOs) and Risks of DNO (rDNOs) Detected in the Follow-Up Period, and Drugs Most Frequently Associated With Them

	DNOs/rDNOs	DNOs	Drugs Associated with DNOs (n)	rDNOs	Drugs Associated with rDNOs (n)
Necessity	42 (29%)	39 (45%)	U (15) I (6)	3 (5%)	C (2)
Nonnecessity	7 (5%)	2 (2%)	U, V (1, each)	5 (8.5%)	H (4)
Nonquantitative ineffectiveness	11 (7.5%)	5 (6%)	L (2)	6 (10%)	T (3)
Quantitative ineffectiveness	39 (26.5%)	21 (24%)	OAD/I (6) D (4)	18 (30%)	D (7) O (5)
Nonquantitative lack of safety	34 (23%)	14 (16%)	D (4)	20 (33.5%)	F (7) A (5)
Quantitative lack of safety	14 (9%)	6 (7%)	D (2)	8 (13%)	D (3)
Total	147 (100%)	87 (100%)		60 (100%)	

A, antiplatelet agent; C, anticoagulants; D, diuretics; F, fizzy (high-sodium) medicines; H, antihistaminic; I, oral iron; L, laxatives; O, omeprazole; OAD/I, oral antidiabetics; T, statins; U, allopurinol; V, venotonic agent.

''inadequate dose, drug regimen, or duration'' (52%); the most prevalent DRP when assessing allopurinol and OAD/insulin was ''insufficiently treated health problem'' (59% and 68%, respectively).

We determined that 94% of DNOs/rDNOs were preventable, and the pharmacist took action in all DNOs/rDNOs detected (Table 5). Eighty-six percent of the interventions were accepted either by clinicians or patients, resulting in a clinical improvement in 39% of the cases and a potential prevention of a new health problem development in 38% of the cases due to these interventions, as seen in the follow-up period (Table 6). When the pharmacist intervention was not accepted (20 cases), 75% of the health problems did not improve (n = 3), the risk of DNO persisted (n = 1) or worsened (n = 7), or the case was considered to be a failure (n = 3: 1 gout attack, 1 hospital admission due to HF decompensation, and 1 death).

Regarding severity, 54% of the DNOs/rDNOs were slight and 40% were moderate. We found 8 (5.5%) serious DNOs/rDNOs (Table 7) that improved or were prevented by pharmacist intervention, except for the single case of nonacceptance of pharmacist intervention, in which the DNO was not solved until the patient was admitted to hospital.

The severity of HF, assessed by CDSS score (CDSS $\geq$2) or NYHA functional class, and age were not independently associated with the number of DNOs/rDNOs. A positive correlation was found between the number of drugs taken and the number of DNOs/rDNOs ($P < .013$; $r = 0.250$).

Discussion

To our knowledge, this is the first study to evaluate DNOs and pharmacist interventions in HF patients. Our observations have several important clinical implications. First, HF outpatients suffer a high number of preventable drug-related morbidity events that may be solved or prevented by a pharmacist included in a multidisciplinary team. Second, those events are more related to comorbidities than to the specific HF syndrome, and they are more frequent in patients who take a higher number of drugs.

Polymedication and older age have often been identified as important DNO risk factors,[29] and these 2 characteristics are present in HF patients. Almost 80% of our patients presented $\geq$1 DNO/rDNO, with up to 6 in some patients. We detected a significant relationship between the number of DNOs/rDNOs per patient and the number of medicines taken, but not the patient's age. We did not uncover a relationship with the severity of the HF disease, perhaps indicating that polymedicated patients, rather than patients more seriously ill due to their HF, should be prioritized for pharmaceutical intervention in this type of population.

From the methodologic viewpoint, there are various definitions and classifications for assessing drug-related morbidity, sometimes mixing the elements of the process of medication use with the outcomes resulting from medicine use.[18] Our classification separated these 2 elements, focusing on outcomes (change in health status) with the DNOs. Interestingly, our study showed a prevalence of events similar to other published data, such as the Minnesota sample (77% in 1,598 patients) and the South Australia sample (90% in 982 patients), 2 large nonHF-specific studies that used a classification mixing elements of process, such as nonadherence and outcomes.[30] This concordance demonstrates that pharmaceutical care practice identifies and resolves drug-related morbidity despite the classification used. In the Minnesota and South Australia samples, patients were included according to selection criteria that may positively influence the existence of these drug-related events, such as polymedication, complicated medication regimens, difficulty with compliance in the South Australian sample, or referred to or requested the services in the Minnesota sample.[30] The strength of our study is that we included all consecutive patients that visited the HF clinic, not having a priori ideal characteristics for pharmaceutical care services.

The distribution of the DNOs/rDNOs was also quite similar among the earlier and the present studies, especially with the Minnesota sample[30] with a mean age of 68 years (74 years in our study) and an average of 6 medications per patient (10 in our population). Some similarities include a 32% versus 28.6% ''necessity of a drug,'' 6% versus 4.8%

Table 4. Drug-Related Problems Associated With DNOs/rDNOs

	Total	DNOs		rDNOs	
	% (n)	% (n)	Drugs (n)	% (n)	Drugs (n)
Erroneous administration of the drug	1.5 (2)	2.2 (2)	E, N (1 each)	0 (0)	—
Personal characteristics	1.5 (2)	2.2 (2)	U, L (1, each)	0 (0)	—
Inappropriate drug storage	0 (0)	0 (0)	—	0 (0)	—
Contraindication	6 (9)	1.1 (1)	L (1)	13.3 (8)	F (6)
Inappropriate dose, drug regimen, and/or duration	22 (32)	10.3 (9)	D (7)	38.3 (23)	D (5)
Duplication	0 (0)	0 (0)	—	0 (0)	—
Dispensing errors	1 (1)	0 (0)	—	1.7 (1)	N (1)
Prescription errors	1 (2)	1.1 (1)	I (1)	1.7 (1)	ACE (1)
Nonadherence	14 (21)	15.4 (13)	I, D (2 each)	13.3 (8)	A (4)
Interactions	0 (0)	0 (0)	—	0 (0)	—
Other health problems that affect treatment	0 (0)	0 (0)	—	0 (0)	—
Adverse effects probability	16 (24)	18.4 (16)	D (2)	13.3 (8)	A (2)
Insufficiently treat health problem	31 (45)	46 (40)	U (14) OAD/I (10) I (5)	8.3 (5)	D (2)
A nonneeded medicine is being taken	2 (3)	1.1 (1)	V (1)	3.4 (2)	H (2)
Lack of monitoring (effectiveness/safety)	1 (1)	0 (0)	—	1.7 (1)	X (1)
Other	3 (5)	2.2 (2)	NSAID, R (1 each)	5 (3)	E, D, P (1 each)

ACE, angiotensin-converting enzyme inhibitors; E, epoetins; N, nitrates; NSAID, nonsteroidal antiinflammatory drugs; P, aldosterone antagonists; R, alendronate; X, l-tiroxine; other abbreviations as in Table 3.

"nonnecessity of a drug," 23% versus 26.5% "quantitative ineffectiveness," 6% versus 7.5% "nonquantitative ineffectiveness," and 6% versus 9.5% "quantitative lack of safety" (all percentages presented as the Minnesota sample versus the current study). The similarity of the results is striking, indicating that DNOs are a common phenomenon in different populations with different diseases in different countries.

Patient adherence has been the main focus of many HF pharmaceutical care studies.[9,10] Interestingly, in the present study, patient nonadherence was not the first, but the fourth cause of DNOs (nonadherence rate of 14%). This could be

Table 5. Pharmacist Interventions to Prevent rDNOs or Solve DNOs, and Most Frequent Drugs Associated With Them

	Total	DNOs		rDNOs	
	% (n)	% (n)	Drugs (n)	n	Drugs (n)
Add a drug	25.5 (37)	37 (32)	U (13)	8 (5)	A (4)
Stop a drug	7 (10)	3.5 (3)	U, V, S (1 each)	13 (8)	H (3)
Substitute a drug	8 (12)	7 (6)	L (2)	10 (6)	NSAID (2)
Reduce the dose	5 (7)	3.5 (3)	D, U, O (1 each)	7 (4)	D (2)
Increase the dose	5 (7)	7 (6)	U (2)	2 (1)	D (1)
Communicate to the doctor that the patient is taking a drug not registered in the medical records	2 (3)	1 (1)	OAD/I (1)	3 (2)	E, D (1, each)
Communicate to the doctor that the patient is not taking a drug registered in the medical records	2 (3)	2 (2)	D (2)	2 (1)	P (1)
Communicate to the patient treatment decisions	4 (6)	4.5 (4)	I, T, ACE, A (1 each)	3 (2)	OAD/I (1) PL (1)
Change the time of administration/ administration with or without food	15 (22)	7 (6)	D (4)	27 (16)	D (5)
Substitute the dosage form	7 (10)	3.5 (3)	I (3)	12 (7)	F (6)
Patient education to improve adherence	6 (9)	5 (4)	U (2)	8 (5)	A (2)
Patient education about nonpharmacologic measures	2 (3)	3.5 (3)	D (2)	0	
Patient education for improved drug administration	1.5 (2)	2 (2)	E, N (1 each)	0	
Suggest a visit to monitor treatment	3 (4)	2 (2)	D, I (1 each)	3 (2)	D, OAD/I (1 each)
Refer to another specialist or general practitioner	7 (11)	11.5 (10)	OAD/I (8)	2 (1)	Inh (1)

Inh, inhalers; Op, opioids; PL, potassium-lowering agents; S, sleep drugs; other abbreviations as in Tables 3 and 4.

Table 6. Health Problem Resolution After Pharmacist Intervention

	% (n)
Solved	24.5 (34)
Improved	11 (15)
Partial improvement	4 (6)
Health problem prevention	38 (52)
Stable	6 (8)
Unimproved	6 (8)
Worsened	7 (10)
Failure	3 (4)
Expired	0 (0)
Risk persistence	0.5 (1)

due to patients in specialized clinics being instructed of the severity of their disease and to their awareness of symptoms and frequent clinic visits. We identified the leading DRP as ''insufficiently treated health problem.'' Frequently in routine clinical practice, there are fewer HF drug prescriptions for patients meeting current clinical practice guidelines than recommended by large randomized clinical trials.[31] In the future, a qualitative study would be useful to obtain a deeper understanding of why some comorbidities also appear to be managed poorly.

The high percentage (85.7%) of acceptance of pharmacist intervention is noteworthy, indicating that the pharmacist influenced the medical specialist's decisions, leading to altered clinical outcomes by improving or potentially preventing the health problems in 83% of the total cases owing to these interventions. More than one-half of the DNOs/rDNOs were considered to be minor, but 5.5% were serious events and were resolved by pharmacist intervention, suggesting that a pharmacist should be considered to be an integral part of an HF team.

Most of the prevalent health problems detected (uncontrolled blood uric acid levels, diabetes, anemia, constipation, and risk of gastric injury) were health problems that are not directly related to HF, and only 22.5% of DNOs/rDNOs were due to HF drugs. We did not uncover a clear explanation for this phenomenon, but it may be that HF specialists focus on the HF syndrome and its treatment and underestimate other comorbidities. However, when a pharmacist revises the medication history and assesses the totality of the drugs taken, he or she is able to identify medication issues beyond HF for these patients.

Table 7. Serious DNO/rDNO Detected

Clinical Problem	n
Uncontrolled blood potassium levels due to spironolactone or calcium polystyrene sulfonate	2
Lack of ACEI in a candidate patient	2
Darbepoetine in a patient with Hb <135	1
Maintenance of high dose of diuretic in a patient with no congestion and renal failure	1
Initiation of acenocumarol without informing the patient about a control visit	1
Aspirin and clopidogrel taken without a gastroprotective agent concomitant with an anticoagulant treatment in a 73-year-old male patient	1
Total	8

We would like to acknowledge some limitations of the present study. There was no control group. However, with the existing evidence of the prevalence of DNOs in other populations,[6–8] we thought it was not ethical having a pharmacist involved in the HF team and not offering the service to one group of patients. In addition, it cannot be assumed that every rDNO detected would in fact develop into a real problem, and the causality between the health problems and the drugs is not proven. However, as a first attempt to assess these unresolved matters, Niquille et al recently demonstrated that drug-related problems are statistically related to clinical outcomes.[20]

In conclusion, the present study demonstrated that the inclusion of a pharmacist in multidisciplinary HF teams should be considered, because it is clinically beneficial for patients and increases HF specialists' awareness of DNOs, especially those beyond HF.

Disclosures

None.

References

1. Rich MW. Multidisciplinary heart failure clinics: are they effective in Canada? CMAJ 2005;173:53–4.
2. Ducharme A, Doyon O, White M, Rouleau JL, Brophy JM. Impact of care at a multidisciplinary congestive heart failure clinic: a randomized trial. CMAJ 2005;173:40–5.
3. Gonseth J, Guallar-Castillon P, Banegas JR, Rodriguez-Artalejo F. The effectiveness of disease management programmes in reducing hospital re-admission in older patients with heart failure: a systematic review and meta-analysis of published reports. Eur Heart J 2004;18:1570–95.
4. Phillips CO, Wright SM, Kern DE, Singra RM, Shepperd S, Rubin HR. Comprehensive discharge planning with postdischarge support for older patients with congestive heart failure: a meta-analysis. JAMA 2004;291:1358–76.
5. McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. J Am Coll Cardiol 2004;44:810–9.
6. Howard RL, Avery AJ, Howard PD, Partridge M. Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study. Qual Saf Health Care 2003;12:280–5.
7. Baena MI, Faus MJ, Fajardo PC, et al. Medicine-related problems resulting in emergency department visits. Eur J Clin Pharmacol 2006;62:387–93.
8. Blix HS, Viktil KK, Reikvam A, et al. The majority of hospitalized patients have drug-related problems: results from a prospective study in general hospitals. Eur J Clin Pharmacol 2004;60:651–8.
9. Varma S, McElnay JC, Hughes CM, Passmore AP, Varma M. Pharmaceutical care of patients with congestive heart failure: interventions and outcomes. Pharmacotherapy 1999;19:860–9.
10. Patel K, Sansgiry SS, Miller L. Pharmacist participation in home health heart-failure programs. Am J Health Sys Pharm 2003;60:2259–60.
11. Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart

failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. Arch Intern Med 1999;159:1939−45.
12. Koshman SL, Charrois TL, Simpson SH, McAlister FA, Tsuyuki RT. Pharmacist care of patients with heart failure: a systematic review of randomized trials. Arch Intern Med 2008;168:687−94.
13. Roughead EE, Barratt JD, Ramsay E, et al. The effectiveness of collaborative medicine reviews in delaying time to next hospitalization for patients with heart failure in the practice setting: results of a cohort study. Circ Heart Fail 2009;2:424−8.
14. Pharmaceutical Care Research Group, University of Granada. Pharmacotherapy follow-up: the Dáder method (3rd rev.; 2005). Pharmacy Practice 2006;4:44−53.
15. Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston: Little, Brown; 1994. p. 253−6.
16. Troughton RW, Frampton CM, Yandle TG, Espiner EA, Nicholls MG, Richards AM. Treatment of heart failure guided by plasma aminoterminal brain natriuretic peptide (N-BNP) concentrations. Lancet 2000; 355:1126−30.
17. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. J Am Coll Cardiol 1993; 22:6−13.
18. Fernández-Llimós F, Tuneu L, Baena MI, Garcia-Delgado A, Faus MJ. Morbidity and mortality associated with pharmacotherapy. Evolution and current concept of drug-related problems. Review. Curr Pharm Des 2004;10:3947−67.
19. Fernandez-Llimos F, Faus MJ. From ''drug-related problems'' to ''negative clinical outcomes.''. Am J Health Syst Pharm 2005; 62:15.
20. Niquille A, Bugnon O. Relationship between drug-related problems and health outcomes: a cross-sectional study among cardiovascular patients. Pharm World Sci 2010;32:512−9.
21. Bentsen N, Bridges-Webb C. An international glossary for general/family practice. Fam Pract 1995;12:267.
22. International Classification of Diseases. Available at. http://www.who.int/classifications/icd/en. Accessed March 31, 2010.
23. Available at: http://medical-dictionary.thefreedictionary.com/intervention. Accessed March 31, 2010.
24. Cipolle RJ, Strand LM, Morley PC. Pharmaceutical care practice. New York: McGraw-Hil; 1998.
25. Real decreto 711/2002, por el que se regula la farmacovigilancia de medicamentos de uso humano. Boletín oficial del estado July 7, 2002.
26. Schumock GT, Thorton JP. Focusing on preventability of adverse drug reactions. Hosp Pharm 1992;27:538.
27. Baena MI, Marín R, Martínez Olmos J, Fajardo P, Vargas J, Faus MJ. Nuevos criterios para determinar la evitabilidad de los problemas relacionados con los medicamentos. Una revisión actualizada a partir de la experiencia con 2.558 personas. Pharm Care Esp 2002;4:393−6.
28. NSAIDs and gastroprotection. MeReC briefing no. 20. National Prescribing Centre. National Health Service 2002.
29. Roten I, Marty S, Beney J. Electronic screening of medical records to detect inpatients at risk of drug-related problems. Pharm World Sci 2010;32:103−7.
30. Rao D, Gilbert A, Strand L, Cipolle R. Drug therapy problems found in ambulatory patients populations in Minnesota and South Australia. Pharm World Sci 2007;29:647−54.
31. Albert NM, Yancy CW, Liang L, Zhao X, Hernandez AF, Peterson ED, et al. Use of aldosterone antagonists in heart failure. JAMA 2009;302:1658−65.