Using Electronic Pharmacy Intervention to Optimize Adherence to Beta-blocker Therapy in Patients With Heart Failure

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When researchers within a VA health care system learned that adherence to recommended beta-blocker therapy in heart failure patients was suboptimal, they sought to determine whether a pharmacist-driven electronic intervention system could influence prescribing practices and, if so, how.

Cardiology research, including landmark trials, has demonstrated that 3 beta-blockers (BBs), bisoprolol, carvedilol, and metoprolol succinate, reduce mortality in heart failure (HF) patients.[1-6] As a result, National Clinical Practice Guidelines strongly recommend using 1 of 3 BBs proven to reduce mortality in all stable patients who have current or prior symptoms of HF and reduced left ventricular ejection fraction (EF), unless contraindicated (Class I, Level of evidence A).[7-8] Additionally, several medications, including angiotensin converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs), diuretics, aldosterone antagonists, digitalis, and hydralazine/nitrates, may be included in the HF patient's treatment regimen.

The Veterans Health Administration Pharmacy Benefits Management Service and the Medical Advisory Panel (VHA PBM-MAP) makes recommendations for the pharmacologic management of chronic HF in primary care practice, which includes BB therapy.[9] The VHA PBM-MAP has outlined recommendations for the use of BBs in VA patients with chronic HF and concomitant left ventricular systolic dysfunction based on national and VHA PBM-MAP clinical practice guidelines for HF.[10] The VHA PBM-MAP states that BB doses should be titrated up, as tolerated, to the doses proven to reduce mortality in clinical trials (Table 1).

Table 1. Target beta-blocker doses in heart failure

Beta-blocker	Target dose
Carvedilol	25 mg twice a day If patient is ≥ 85 kg, titrate as tolerated to 50 mg twice a day
Metoprolol succinate	200 mg daily
Bisoprolol	10 mg daily

WHAT THE LITERATURE SAID

Unfortunately, trials and VA PBM data show that prescribing practices have not kept up with current practice guidelines.[11,12] In 2008, Rector and colleagues performed a retrospective cohort study that characterized the prescribing of carvedilol vs metoprolol succinate for predominantly elderly (≥ 65 years old) veterans with HF and compared the time to first hospitalization or death. The study involved a total of 26,112 veterans nationwide: 17,429 veterans in the carvedilol group and 8,683 in the metoprolol succinate group. Within this study, 91% of carvedilol patients and 85% of metoprolol succinate patients refilled their prescriptions. Of these patients, 41% of carvedilol and 26% of metoprolol succinate patients received higher doses when compared to the initial prescription.

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Only 22% of carvedilol (median time, 24 months) and 4% of metoprolol succinate (median time, 14 months) patients reached their target dose. The average dose indicated on the last prescription was 25% of the target dose in both groups. The average time to first hospitalization was 4.2 months for the metoprolol succinate patients and 5.7 months for the carvedilol patients. The risk-adjusted metoprolol succinate-to-carvedilol hazard ratios were 0.99 (95% CI) for hospitalization/death, and 0.91 for death alone.[12]

Direct pharmacotherapy interventions have been shown to be most successful in helping patients with HF achieve goal doses of BBs.[13-15] In 2003, Ansari and colleagues conducted a randomized, controlled trial to evaluate strategies to improve guideline adherence and use of BBs in HF. The study comprised 169 HF patients with an EF ≤ 45% and no contraindications to BBs. Primary care providers (PCPs) were randomly assigned to 1 of 3 interventions: the provider education (control group); the provider/patient notification group using computerized provider reminders and patient letters advocating BBs; or a nurse facilitator group in which a supervised nurse initiated and titrated BB therapy. The primary outcome for this study was the percentage of patients initiated, or titrated upward, then maintained on a BB. Study results showed the nurse facilitator intervention to be the most successful. In this group, 67% of patients reached the primary outcome compared to only 16% of patients in the provider/patient notification group and 27% in the provider education group. The proportion of patients on target BB doses at the end of the study (median 12 months follow-up) was highest in the nurse facilitator group (43%) vs the provider education group (10%) and the provider/patient notification group (2%).[13]

OUR PURPOSE

Clinical pharmacists at the Southern Arizona VA Healthcare System (SAVAHCS) have developed strong collaborative practice relationships with PCPs. At the PCP's request, pharmacists co-manage patients who have hypertension, hyperlipidemia, diabetes, and other disease states using a collaborative practice agreement. Currently, pharmacists at SAVAHCS are not directly involved in managing HF in the primary care setting.

The electronic medical record (EMR) system is an integral part of clinical practice in the VA. The system provides staff members with an effective and efficient mode of communication in the medical record through view alerts. View alerts are a tool within the system that notifies the health care provider when a laboratory, imaging result, or note from another clinician requires attention.

With an advanced collaborative clinical pharmacy practice model and EMR system, we conducted our study to determine whether a pharmacist-driven electronic intervention system could influence prescribing practices. We specifically focused on whether pharmacists could influence the titration of BB doses in HF patients.

METHODS

We conducted our study in 2 phases. Phase 1 involved a medication use evaluation (MUE) of HF patients eligible for a BB dose increase according to the HF guidelines and baseline characteristics of the patients. Phase 2 examined the impact of an electronic pharmacy intervention on BB prescribing in HF patients in accordance with the guidelines.

Our protocol was approved by the SAVAHCS Research and Development Committee and the University of Arizona Institutional Review Board.

Table 2. Pharmacy intervention: electronic progress note

Pharmacy chronic heart failure (HF) beta-blocker review

According to VHA recommendations based on National Clinical Practice Guidelines, the following are beta-blocker recommendations for patients with systolic HF.
(Only relevant information will be included for the medication the patient is currently on: metoprolol succinate or carvedilol.)

Metoprolol succinate	Carvedilol
• Initial dose 12.5 mg once daily ≥ NYHA[a] class III HF; 25 mg once daily < NYHA class III HF • Double dose every 2 weeks until target dose • Target dose 200 mg daily	• Initial dose 3.125 mg twice a day • Dose should be doubled at a minimum of every 2 weeks to the target dose • Target dose 25 mg twice a day; titrate as tolerated to 50 mg twice a day if patient is ≥ 85 kg

A: Patient not on optimal beta-blocker therapy and appears to have no contraindications to an increased dose.
P: Consider increase in (metoprolol succinate/carvedilol) to _____ .

[a]New York Heart Association.

The procedures we followed complied with the ethical standards of the SAVAHCS subcommittee on human subjects.

Phase 1: Medication use evaluation (screening)

In Phase 1, we aimed to establish baseline characteristics of patients, identify indications for nonadherence to BB guidelines, and determine eligibility for Phase 2. We used a computer query of EMRs between June 30, 2008, and July 1, 2009, to generate a list of study subjects meeting the following inclusion criteria: men and women ≥ 18 and < 90 years old and 2 ambulatory care visit ICD-9 (International Classification of Disease 9th Clinical Modification) codes for nondiastolic HF. The ICD-9 codes included were 428.xx (except for 428.3x, which is diastolic); 402.01; 402.11; 402.91; 404.01; 404.11; and 404.91. Patients had to have an active BB prescription for metoprolol succinate or carvedilol at a suboptimal dose as defined by the VHA PBM-MAP guideline, and an active prescription for an ACEI or an ARB. Patients were excluded if they were enrolled in the Care Coordination Home Telehealth (CCHT) program; had an EF ≥ 40%; or if SAVAHCS was not their primary VA medical center. CCHT program patients are followed intensively through technology in the patient's home and do not represent the typical VA primary care patient, and the VHA PBM-MAP guideline is specific for patients with an EF < 40%. With the help of Microsoft Excel, eligible patients were randomized into blocks of 50 for screening until 25 patients were randomized into each group for Phase 2.

We collected data regarding age; sex; EF; dose of ACEI/ARB; prescriber type (specialist vs PCP); ambulatory blood pressure (BP) and heart rate (HR); and concomitant HF medications as part of the Phase 1 screening process. We also noted whether patients had previously tried—and failed—a higher dose of BB, and indicated the reasons for failure, if applicable.

We followed the VHA PBM-MAP recommendation for the use of BBs in HF to evaluate the appropriateness of prescribing practices and patients' therapy at SAVAHCS. The primary endpoint for Phase 1 was to identify patients who were eligible for a BB dose increase according to the VHA PBM-MAP HF guideline, which was the qualifier for Phase 2 (Intervention) of our study. Secondary endpoints were to characterize reasons why patients were not on optimal BB doses according to the HF guideline.

Phase 2: Intervention

In Phase 2, we sought to evaluate the efficacy of electronic pharmacy intervention in HF patients. All members of the SAVAHCS provider e-mail group and all care line chiefs were given the VHA PBM-MAP *Recommendations for the Use of Beta-Adrenergic Blockers in VA Patients with Chronic Heart Failure with Left Ventricular Systolic Dysfunction*[10] approximately 75 days before the Intervention to increase awareness of the guideline. Phase 2 patients were those deemed eligible for a BB dose increase in Phase 1 screening, who also had an average HR > 60 beats per minute and an average systolic BP > 100 mm Hg

Table 3. Baseline patient characteristics (average)		
	Intervention	Control
Male (%)	100	92
Age (years)	71	71
Ejection fraction (%)	23	25
Age of echocardiogram (d)	792	574
Total daily dose – metoprolol succinate (mg)	50	110
Total daily dose – carvedilol (mg)	25	25
Heart rate (bpm)	72	71
Systolic blood pressure (mm Hg)	128	123
Diastolic blood pressure (mm Hg)	74	71
Concomitant heart failure medications (%)		
ACEI	74	78
ARB	26	24
Optimal dose ACEI/ARB[a]	27	18
Diuretic	80	84
Isosorbide dinitrate	24	16
HMG-CoA reductase inhibitors	22	22
Spironolactone	4	12
Digoxin	0	4
Prescriber type (No. BB prescriptions)		
Primary care physician	16	18
Nurse practitioner	4	3
Cardiologist	3	2
Cardiology nurse practitioner	2	2

ACEI = angiotensin converting enzyme inhibitors; ARB = angiotensin II receptor blockers; BB = beta-blocker; HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A.
[a]Optimal dose defined by VHA chronic heart failure guidelines.

from the last 3 ambulatory care readings. Patients were excluded during Phase 1 screening if they failed a previous trial at the goal BB dose; had a reason for not titrating the BB that was documented in the EMR; were undergoing active BB titration; or did not have the required vital signs available.

The Intervention consisted of a pharmacy-driven electronic progress note (Table 2). The progress note contained pertinent information for the provider to review, as well as a recommendation to increase the dose of the patient's current BB. The progress note was placed in the patient's EMR and sent as a view alert to the provider who prescribed the BB for co-signature. If the patient was no longer being followed by the prescribing provider, the patient's current PCP or cardiologist was designated the co-signer and received the view alert. The type of provider to which the intervention was addressed was recorded. Control group patients had no further actions taken beyond the initial group e-mailing of the HF guideline.

Medical records were reviewed 30 days after the intervention to determine whether any action was taken by the provider in response to the pharmacy intervention. The primary endpoint was to compare the intervention and control groups on whether an action was taken; the secondary endpoint was to characterize the type of action taken.

Table 4. Medication use evaluation exclusion criteria (n = 210)

Exclusion	No. patients (%)
EF ≥ 40%	134 (64)
Enrolled in CCHT program	58 (28)
EF not listed	15 (7)
Not an SAVAHCS patient	3 (1)

CCHT = Care Coordination Home Telehealth; EF = ejection fraction; SAVAHCS = Southern Arizona VA Healthcare System in Tucson.

Table 5. Reasons for suboptimal beta-blocker doses in heart failure patients (n = 57)

Reason	No. patients (%)
Low heart rate	15 (26)
Low blood pressure	14 (25)
Failed titration	8 (14)
Pulmonary disease	5 (9)
Active titration	4 (7)
Fatigue	3 (5)
Dizziness	3 (5)
Documented noncompliance	3 (5)
Other	2 (4)

DATA ANALYSIS

In Phase 1 (MUE), descriptive statistics, such as numerical counts and percentages, were used to compare the baseline differences between patients. In Phase 2 (Intervention), the primary endpoint was compared using Fisher's exact test. Secondary outcomes were also analyzed using Fisher's exact test, which included actions taken to increase the BB dose between groups. The groups were also compared on the number and percentage of each action reported. Descriptive statistics were used for the types of prescribers addressed.

PATIENT CHARACTERISTICS

Baseline patient characteristics in the intervention and control groups were well matched, except for the average total daily dose of metoprolol succinate and the age of their echocardiograms (ECHOs). Patients were predominantly male, around 71 years of age, with EFs of approximately 25% (Table 3). Patients were taking typical concomitant medications for HF. All were taking an ACEI or an ARB as required by the inclusion criteria, with most patients in both groups receiving an ACEI. There was a large number of patients in both groups who were not taking optimal doses of ACEIs or ARBs as defined by the HF guideline. Use of other HF medications in the intervention and control groups was evenly matched, except for spironolactone use.

RESULTS

Of the 317 patients who met our inclusion criteria, 66% were excluded from Phase 1, mainly due to an EF ≥ 40% (Table 4). The remaining 107 patients were evaluated. Of those 107, 50 patients met the primary endpoint (that is, eligibility for BB dose increase and pharmacy intervention) and were included in Phase 2. A low BP or HR was the primary reason identified for patients taking suboptimal BB doses. Other reasons for suboptimal doses were previous failure of BB dose titration; documented contraindications to BB dose escalation, such as pulmonary disease; or current titration of BB doses (Table 5).

Most of the prescriptions for metoprolol succinate and carvedilol were written by PCPs. Most of the interventions placed were directed toward PCPs, because they wrote most of the prescriptions. Of the 25 interventions placed, 19 providers took action on the intervention vs 1 provider in the control group.

Secondary endpoints of Phase 2 were characterized by a majority of providers (n = 18; 72%) in the intervention group who prescribed an increased BB dose or took actions likely to result in BB dose increases. Only 1 provider disagreed with the electronic pharmacy intervention. Significantly more providers in the intervention group (72%), vs the control group (4%), took actions to optimize BB doses ($P < .0001$) (Figure).

A large number of providers chose to schedule future appointments as opposed to immediately increasing the BB dose. Two PCPs who wrote increased BB dose prescriptions also placed pharmacy consults for follow-up of the dose change. One PCP who scheduled a future appointment also placed a pharmacy consult. Therefore, of the 22 total actions taken, 3 providers took 2 separate actions, which resulted in 19 unique responses to the intervention.

DISCUSSION

Our study demonstrated that an electronic pharmacy intervention can optimize BB therapy in HF patients. Provider response to the electronic pharmacy intervention was overwhelmingly enthusiastic. Consideration should be given to expanding

the roles of pharmacists in primary care to include HF management within their scope of practice. In contrast to the study conducted by Ansari and colleagues in 2003,[13] our study showed that provider notification using computerized alerts to recommend an increase in BBs was successful when accompanied by 3 items. These are 1) the prescribing guidelines of the VHA PBM-MAP; 2) patient-specific data that supports the dose increase; and 3) patient-specific titration recommendations in accordance with the guidelines.

Study limitations

Several limitations within our study, however, warrant consideration. Our study was conducted on the assumption that the reported EF percentage was consistently accurate. Although a difference was seen in the age of ECHOs between groups, both groups had ECHOs > 500 days old. In addition, the intervention and control groups were well matched, except for the average total daily dose of metoprolol succinate, and spironolactone use. The discrepancy in the baseline metoprolol succinate dose may have disproportionately prompted prescribers in the intervention group to act, because the baseline average metoprolol succinate dose was lower in the intervention group. Control group patients may have had more advanced HF. More control group patients were taking spironolactone, and they had a higher baseline average dose of metoprolol succinate. Because HF class was not measured, it could not be definitively determined.

Another limiting factor was that adherence and/or refill persistence for BBs was not measured within the study population. Therefore, we cannot determine whether the patients in this study complied with their BB therapy.

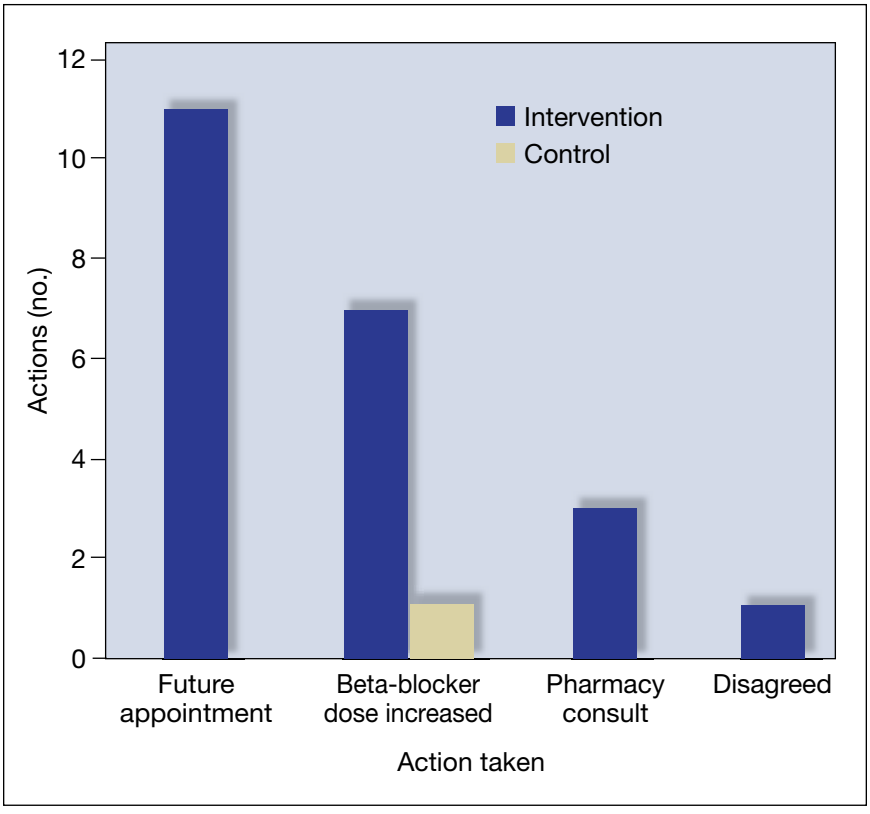

Figure. Types of action taken.

Action was taken to schedule future appointments instead of immediately increasing the BB dose. Shortly after interventions were made, primary care teams at SAVAHCS hired several new staff members and experienced shifts in patient panels. This meant that staff members were receiving electronic interventions for patients they had not seen previously. Lack of familiarity with patients likely prompted many providers to schedule future appointments to evaluate the appropriateness of a BB dose escalation as opposed to immediately writing new prescriptions. If our study was not limited by a short follow-up interval (30 days), actions likely to result in a BB dose increase, such as the scheduling of future appointments, could have been monitored to determine whether BB doses were actually increased at subsequent appointments.

Further examination of ACEI and ARB dosing in HF patients may be warranted, because most of the study patients were not taking the optimal doses of ACEI/ARB prescribed for HF. Although they were not taking optimal doses as prescribed by the guidelines, many patients in this study were taking the maximum dose of BB that they could tolerate. The same may be true for the ACEI/ARB prescriptions noted in our study.

The ability to generalize our study's results beyond the VA system is limited. The VA has an integrated EMR system and a homogeneous patient population. Site-specific collaboration between pharmacists and PCPs also may have contributed to the success of our intervention and, subsequently,

may further limit our ability to generalize our results to other settings.

CONCLUSION

When we learned that adherence to recommended BB therapy in patients with HF was suboptimal, we sought to determine whether a pharmacist-driven electronic intervention system could influence prescribing practices. Despite some limitations, our results showed that pharmacy-driven electronic intervention was, in fact, successful for improving adherence to HF guidelines in a facility that has a strong clinical pharmacy practice in primary care and an established EMR system, such as that within the VA system.

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