Effect of a Clinical Pharmacist–Managed Service on Blood Pressure in an Underserved Population With Resistant Hypertension

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Abstract

Background. Evidence indicates pharmacist-managed hypertension clinics are beneficial in reducing blood pressure (BP). There is currently no evidence evaluating the effect of pharmacist-managed resistant hypertension clinics in a medically underserved patient population. **Objective.** To determine the impact of a pharmacist-managed resistant hypertension service on BP in a medically underserved population. **Methods.** This was a prospective cohort study evaluating 12 medically underserved patients enrolled in a pharmacist-managed resistant hypertension service at the St Louis County Department of Health. BP was measured in clinic and at home. Follow-up occurred biweekly by phone and in clinic at least monthly while uncontrolled. This study was approved by the St Louis College of Pharmacy Institutional Review Board and St Louis County Department of Health director for clinical and research services. Primary outcome of change in home systolic BP and secondary outcomes of change in home diastolic BP and clinic systolic and diastolic BP were evaluated. **Results.** Twelve patients were included in the analysis (2 patients did not receive home BP monitors). Home systolic BP was reduced from the first encounter, 140 (12) mm Hg, to last contact, 130 (15) mm Hg ($P = .01$). Clinic systolic BP also decreased significantly from the first encounter, 152 (10) mm Hg, to last contact, 136 (17) mm Hg ($P = .004$). Clinic BP goal and home BP goal was attained by 30% and 40% of participants, respectively. **Conclusions.** A pharmacist-managed resistant hypertension service is effective in significantly reducing BP in medically underserved patients.

Keywords

clinical pharmacy, hypertension, antihypertensives, pharmaceutical care, ambulatory care

Introduction

Resistant hypertension is defined as blood pressure (BP) that remains above goal despite use of 3 antihypertensive agents from different classes, one of which should be a diuretic, with all agents at maximal doses. Thus, patients who require 4 or more BP medications to achieve their goal BP are considered to have resistant hypertension.¹ Patients with resistant hypertension are at high risk for adverse outcomes including cardiac, vascular, and renal complications.¹ According to the 2003–2008 National Health and Nutrition Examination Survey epidemiological data, among adults in the United States with hypertension, approximately 12% met the criteria for resistant hypertension, representing an increase of 5.5% from 1994 to 1998 and 8.5% from 1999 to 2004.^{2,3} Several known risk factors for resistant hypertension have been identified including age, high baseline BP, obesity, chronic kidney disease, diabetes, left ventricular hypertrophy, and female gender.¹ Patients with resistant hypertension are more likely than those with controlled

hypertension to have a reversible secondary cause such as sleep apnea, renal parenchymal disease, renal artery stenosis, and primary aldosteronism.¹

Treatment of resistant hypertension should begin with identifying possible contributing and secondary factors. Lifestyle modifications including weight loss; regular exercise; ingestion of a high-fiber, low-fat, low-salt diet; and moderation of alcohol intake should be combined with

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pharmacological drug therapy.¹ These lifestyle interventions can lead to a reduction in systolic BP (SBP) by 4 to 11 mm Hg and diastolic BP (DBP) by 2 to 6 mm Hg.¹ Pharmacological therapy is selected to ensure that all possible mechanisms leading to resistance are addressed. Most commonly, patients with resistant hypertension experience inappropriate volume expansion making diuretics a standard component of the antihypertensive regimen.¹ Diuretics have provided significant BP control when used in combination with other antihypertensive medications for resistant hypertension.^{4,5} Garg and colleagues found that 53% of patients with resistant hypertension were controlled to goal when diuretic therapy (a component of a 4-drug regimen) was intensified and optimized.⁴

The most common secondary cause of uncontrolled hypertension identified is medication nonadherence (defined as patients taking less than 80% of prescribed doses).⁶ Nonadherence rates in patients with resistant hypertension have ranged from 10% to 65%.⁷ Evidence examining adherence has been measured using various mechanisms including interviews, pill counts, and serum drug levels.^{6,7} While most of the trials examining adherence include patients referred to a specialty clinic, few describe the role and impact of a pharmacist-led effort.^{4,8-11}

Resistant hypertension studies are often limited and confounded by the presence of multiple disease processes (eg, sleep apnea, diabetes, chronic kidney disease, atherosclerotic disease) and their associated medical therapies. Patients with resistant hypertension often have a high risk of cardiovascular events, which generally precludes safe withdrawal of medications. Additionally, trials exploring resistant hypertension outcomes are limited by a small sample size.

Interprofessional teams offer diversity of expertise and are often used as an adjunct to usual care in the treatment of resistant hypertension. Rinfret and colleagues evaluated a multidisciplinary team, including nurses, physicians, and pharmacists.¹² This team intervention included communication with patients by telephone, email, and in person during office visits. Compared to usual care, the intervention group had a greater reduction in BP and a greater percentage of patients achieve their BP goal. Evidence indicates there can be a significant benefit in working with other disciplines in the management of hypertension.^{13,14}

The impact of a pharmacist, in particular, on BP has also been investigated.^{15,17} Studies have demonstrated that pharmacists provide a greater benefit on lowering BP, achieving BP goals, choosing evidence-based therapy, and increasing patient satisfaction of care compared to usual care.¹⁵⁻¹⁸ When looking specifically at resistant hypertension management, pharmacists have demonstrated similar clinical benefit. Patients with resistant hypertension who receive a pharmacist intervention achieve lower BPs and a reduction in BP, urgent care visits, and hospitalizations.^{13,14}

Black patients often develop hypertension at a younger age and have more severely elevated BP.¹⁹ Studies evaluating the impact of pharmacist management of hypertension have not reported race.¹²⁻¹⁴ Race was reported in the investigation of pharmacist-led resistant hypertension care, but black patients represented less than 8% of the total study population.¹⁵ It is unknown if pharmacist services in a primarily black population would produce different results. Although limited evidence is available to assess BP control in indigent hypertensive patients, the information available indicates indigent patients treated by a clinic focusing on hypertension management leads to a greater reduction in BP than that of a general medicine clinic.²⁰⁻²²

While there is substantial evidence regarding the benefit of pharmacist-run hypertension clinics, there is limited evidence for the impact of a pharmacist-managed resistant hypertension clinic and limited evidence available of the impact in an indigent, minority patient population. There is, therefore, a need to evaluate the impact of a pharmacist-managed resistant hypertension clinic in a medically underserved patient population.

Methods

Setting and Patient Population

The St Louis County Department of Health offers primary care services for medically underserved residents of St Louis County. Patients receiving primary care services at the North Central Community Health Center, which was the site selected for this study, have medical coverage through state or federal programs or are uninsured. The majority of patients (>80%) are black. St Louis College of Pharmacy institutional review board and the director for clinical and research services at the St Louis County Department of Health approved the study. All patients receiving primary care at the North Central Health Center were eligible for inclusion in the study. Patients age ≥ 18 years were eligible for enrollment in the clinical pharmacy service if they had resistant hypertension, defined as having uncontrolled BP despite the use of 3 or more antihypertensive medications, including a diuretic, all of which were at optimal doses. Patients were still considered eligible for inclusion in the study if they were unable to take a diuretic due to reasons such as an allergy or contraindication. Participants signed a written informed consent document and HIPAA authorization form.

Design

This was a prospective cohort study designed to assess the effect of a clinical pharmacy-managed resistant hypertension service on BP. The primary outcome was change in home SBP from baseline to study end. Secondary outcomes

Table 1. Blood Pressure Goals.

Patient Population	Home BP Goal ²⁵	Clinic BP Goal ^{24,25}
No compelling indications	<135/85 mm Hg	<140/90 mm Hg
DM, CKD, high CAD risk ^a , PAD, CAD, history of stroke	<130/80 mm Hg	<130/80 mmHg
Left ventricular dysfunction	<120/80 mm Hg	<120/80 mm Hg

Abbreviations: BP, Blood pressure; DM, diabetes mellitus; CKD, chronic kidney disease; CAD, coronary artery disease; PAD, peripheral arterial disease.

^aFramingham 10-year risk score >10%

included change in clinic and home SBP and DBP, number of medications, and encounters. Patients were screened for enrollment during an encounter with their primary care provider, and patient eligibility was communicated to the provider with a request for referral. Patients identified as having a secondary etiology of hypertension were not eligible for inclusion. The first postreferral encounter with the clinical pharmacists (enrollment visit) education was provided on hypertension, including a review of the basic disease process, potential complications, BP goals, treatment options, nonpharmacologic management, and medication-specific information. Nonpharmacologic management included education on weight loss, sodium restriction, DASH diet, physical activity, and moderate alcohol consumption. At this encounter, patients were also given an Omron 7 Series Upper Arm Blood Pressure Monitor BP 760 (Omron Corporation, Kyoto, Japan) and advised to obtain home BP readings in the morning and in the evening on a daily basis. The monitor accommodates patients requiring standard or large cuffs; patients did not receive monitors if their arm circumference was too large for the cuff (>17 in.). Clinic BP goals were set according to the then current guidelines, JNC7, AHA, and AHA/ASH/PCNA.²³⁻²⁵ Home BP goals were determined based on AHA recommendations.^{24,25} Goals are summarized in Table 1. Follow-up occurred biweekly by phone encounters, and participants were seen in clinic at least monthly while uncontrolled. Once controlled patients were followed by phone monthly and in clinic every 6 months. Monitoring included BP and heart rate at 2-week intervals and periodic laboratory monitoring of renal function and serum electrolytes as indicated by regimen. Medication changes, including initiation, dose change, or discontinuation, were implemented at each encounter until patient-specific goals were consistently met. Medication and laboratory orders were initiated by the pharmacist based on a clinical protocol that was approved by referring physicians. When adding new therapies, angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), diuretics, calcium channel blockers, and β -blockers were initiated

based on compelling indication (Figure 1) and maximized. Thereafter, secondary antihypertensives including spironolactone and doxazosin were utilized (Figure 2). Patients without contraindications were initiated on spironolactone. Chronotherapy administration (ie, dosing at least one antihypertensive at bedtime) was implemented for patients with diabetes. Data collection occurred from January 2011 through May 2011.

Statistical Analysis

Descriptive statistics were used to analyze patient demographics. Continuous outcomes were assessed using Student's *t* test with last observation carried forward. Participants were included in the analysis if they successfully completed 2 encounters, including enrollment and one postenrollment encounter. Statistical analyses were performed using Microsoft Excel, 2010 Version 14, and SPSS, Version 18. A sample size of 15 was calculated in order to achieve 80% power allowing for a 5% α and a standardized effect size of 0.8 (anticipated change in SBP of 10 mm Hg with standard deviation of 12 mm Hg).

Results

A total of 12 participants were included in the analysis. Two patients did not receive home BP monitors based on arm circumference. Baseline characteristics are presented in Table 2. Mean age of participants was 57 years (SD 8), and 83% were female. The most common comorbid conditions were diabetes mellitus, 83%, and chronic kidney disease (CKD), 25%. Baseline and end of study medication use is displayed in Table 3. Of the 3 participants with documented allergies, 1 patient had an allergy to ACEIs. The second patient had documented allergies to ACEIs, thiazide diuretics, and sulfa medications, and was therefore not treated with a diuretic. The third patient had documented allergies to ARBs and thiazide diuretics. The majority, 92%, had a clinic BP goal of <130/80 mm Hg, and 92% had a home BP goal of <130/80 mm Hg.

Mean BP the day of screening, referral, and enrollment are outlined in Table 4. There was a mean of 4 (SD 2.9) phone encounters, 2.5 (SD 1.1) clinic visits, and a mean of 138 (SD 59) days enrolled in the service. For the primary outcome, a significant reduction was seen in home SBP from the first encounter to last contact (140 [SD 12] mm Hg vs 130 [SD 15] mm Hg; $P = .01$; Table 5). Significant reductions in BP were also demonstrated in secondary outcomes. Clinic SBP decreased from the first encounter to last contact (152 [SD 10] mm Hg vs 136 [SD 17] mm Hg; $P = .004$). Clinic DBP decreased from the first encounter to last contact (84 [SD 12] mm Hg vs 73 [SD 10] mm Hg; $P = .01$). The mean first 2 days of home SBP decreased compared to the mean last 2 days (144 [SD 14] mm Hg compared to 128

Figure 1. Primary antihypertensive treatment algorithm.

Figure 2. Secondary antihypertensive treatment algorithm.

mm Hg; $P = .002$). Mean first 2 days of home DBP decreased compared to mean last 2 days (82 [SD 12] mm Hg vs 74 [SD 7] mm Hg; $P = .01$). Clinic BP goal was attained by 33%, and home BP goal was attained by 40%. When looking at patients with diabetes, 30% attained their clinic BP goal and 40% attained their home BP goal.

A total of 35 interventions were made during the study period with an increase in antihypertensive doses being the most common (51%). Other interventions included the addition of new therapy (23%), nonpharmacologic therapy education (20%), medication discontinuation (3%), and decreases in antihypertensive doses (3%). At baseline, participants were treated with an average of 4.25 antihypertensive medications. By end of study this increased to an average of 4.6 antihypertensives per participant; this difference was not statistically different.

Discussion

Our study was able to demonstrate significant reduction in BP from baseline to follow-up (mean of approximately 4 months) in patients enrolled in a clinical pharmacist-managed resistant hypertension service. These significant findings were apparent despite the fact that we were unable to achieve the estimated sample size needed to achieve statistical power. While baseline BP measurements were similar across studies, the magnitude of change we observed in clinic and home BPs in this study was greater than the predicted change and the variability was similar to our estimate; therefore, we were able to demonstrate statistically significant differences with a smaller than estimated sample size.^{15,26}

Our study population differed significantly from that of other published studies evaluating pharmacist-based interventions. Our population was primarily (>80%) black and the majority (>80%) had diabetes. Carter et al described the

Table 2. Baseline Characteristics, N = 12.

Variable	Findings
Age, mean years (SD)	57 (8)
Female, n (%)	10 (83%)
Race, n (%)	
Black	10 (83%)
Caucasian	2 (17%)
Insurance, n (%)	
Medicare	5 (42%)
Medicaid	2 (17%)
Self-pay	5 (42%)
BMI, kg/m ²	38
Tobacco use, n (%)	4 (33%)
Alcohol use, n (%)	2 (17%)
Illicit drug use, n (%)	0
CKD, n (%)	3 (25%)
DM, n (%)	10 (83%)
ACS, n (%)	1 (8%)
Stable angina, n (%)	0
CHD risk equivalent, n (%)	2 (17%)
LVD, n (%)	1 (8%)
TSH, mIU/L (SD)	1.98 (1.25)
Plasma glucose, mg/dL(SD)	117 (42)
TChol, mg/dL (SD)	180 (42)
LDL, mg/dL (SD)	107 (39)
TG, mg/dL (SD)	129 (51)
HDL, mg/dL (SD)	47 (11)
A1c, % (SD)	6.8 (0.6)
Albuminuria, n (%)	4 (33)
GFR, mL/min (SD)	84 (24)

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; CHD, coronary heart disease; CKD, chronic kidney disease; DM, diabetes mellitus; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVD, left ventricular dysfunction; TChol, total cholesterol; TG, triglycerides; TSH, thyroid-stimulating hormone.

impact of a pharmacist-physician collaborative approach on BP in a randomized, controlled study.²⁶ The population enrolled was primarily (>80%) Caucasian and had a low frequency (<30%) of diabetes. Similarly, a study by Green et al investigated the impact of home BP monitoring and pharmacist care on BP outcomes.¹⁵ The subjects included in this study were primarily Caucasian (>80%), and those with diabetes were excluded from participation. It is unclear whether these differences in demographics explain the greater magnitude of BP change observed, but it is one possible explanation.

The intervention in our study was multifactorial including pharmacist encounters that incorporated home BP monitoring and frequent follow-up. It is possible that the multiple components of the intervention were additive or synergistic in effect. However, in the Green et al study, 1 of 2 control groups received care that included home BP

Table 3. Medication Use at Baseline and End of Study.

Antihypertensive	Baseline, n (%)	End of Study
ACEI	9 (75)	8 (67)
Benazepril	1 (8)	2 (17)
Enalapril	1 (8)	1 (8)
Lisinopril	7 (58)	5 (42)
ARB	4 (33)	2 (17%)
Losartan	3 (25)	2 (17%)
Olmesartan	1 (8)	0
β-Blocker	10 (83)	9 (75)
Atenolol	4 (33)	2 (42)
Carvedilol	1 (8)	1 (8)
Carvedilol cr	1 (8)	0
Metoprolol	4 (33)	6 (50)
Dihydropyridine calcium channel blocker	10 (83)	11 (92)
Amlodipine	10 (83)	11 (92)
Nondihydropyridine calcium channel blocker	0	0
Diltiazem	0	0
Verapamil	0	0
Diuretic	11 (92)	9 (75)
Furosemide	3 (25)	3 (25)
Hydrochlorothiazide	8 (67)	6 (50)
Aldosterone antagonist	0	4 (33)
Spironolactone	0	4 (33)
α ₁ -Blocker	2 (17)	2 (17)
Doxazosin	2 (17)	2 (17)
Vasodilator	2 (17)	3 (25)
Hydralazine	2 (17)	3 (25)
α ₂ -Agonist	2 (17)	2 (17)
Clonidine	2 (17)	2 (17)

Abbreviations: ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

monitoring and web-based communication, while the intervention group received those services with pharmacist care as the only addition.¹⁵ The control group did not demonstrate the degree of improvement observed in the pharmacist-intervention cohort. While the components may be additive, the Green study supports the involvement of a clinical pharmacist as a critical factor in the success of an intervention.

While this study did not include the proportion of patients achieving evidence-based BP goal as a primary outcome, these data were reported. It is important to note that over 90% of the enrolled subjects were considered to have a clinic BP goal of <130/80 mm Hg at the time of the study. Contemporary guidelines^{27,28} no longer endorse that BP goal for patients with diabetes and only disease-specific guidelines support that goal in those with proteinuric CKD.²⁹ All enrolled patients would still have met the definition of resistant hypertension at baseline based on new

Table 4. Baseline Blood Pressure (N = 12).

	Mean SBP, mm Hg (SD)	Mean DBP, mm Hg (SD)
Day of screening	158 (29)	80 (13)
Day of referral	159 (15)	84 (12)
Day of enrollment	152 (10)	84 (12)

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table 5. Change in Home and Clinic Blood Pressure From First Encounter to End of Study (N = 10).

N = 10	First Encounter	End of Study	P Value
Change in home SBP	140 (12) mm Hg	130 (14) mm Hg	.005
Change in home DBP	80 (10) mm Hg	77 (10) mm Hg	.07
Change in first 2 days home SBP to last 2 days home SBP end of study	144 (14) mm Hg	128 (12) mm Hg	.002
Change in first 2 days home DBP to last 2 days home DBP end of study	82 (12) mm Hg	74 (7) mm Hg	.01
N = 12	First Encounter	End of Study	P Value
Change in clinic SBP	152 (10) mm Hg	136 (17) mm Hg	.004
Change in clinic DBP	84 (12) mm Hg	73 (10) mm Hg	.01

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

guidelines. However, had the study been conducted more recently, it is likely that medication adjustments would reflect the less aggressive goals in these guidelines and that a less pronounced BP change would be demonstrated.

It is interesting to note the difference in home BPs and clinic BPs observed in our study. While both analyses indicate significant improvements and similar magnitude of change in BP, measurement of clinic BP alone would indicate continued need for adjustment in those with SBP goal of <130 mm Hg while home BP values do not.²⁵ This finding is consistent with other studies and supports the recommendation that home BP measurements be used more routinely to evaluate for the presence of white coat hypertension and for ongoing monitoring and adjustment. In our study, we were able to control the consistency and quality of home BP monitors used, while this likely represents a challenge when attempting to use these data in clinical practice. Traditional office BP measurements do not consistently

provide a completely accurate assessment of BP and have been shown to underestimate BP control 33.4% of the time.³⁰ While some of the discrepancy may be due to the white coat phenomenon, some is also likely due to the frequency of office measurements occurring during the peak effect of many antihypertensive medications.

There are several potential intervention-specific explanations for the successful BP reduction observed in our small cohort of patients followed by clinical pharmacists. Pharmacists in our setting are able to focus significant time on BP management. Office encounters are 30 to 60 minutes in length. This is in contrast to the typical, busy primary care physician that is often faced with multiple patient complaints and comorbidities and short visit times. Clinical inertia is a well-documented phenomenon associated with a lack of BP control.^{31,32} The pharmacists' ability to focus significant time on hypertension management in this specialty service combined with the availability of home BP values likely decreased the risk of clinical inertia. The frequency of encounters is also a likely contributor with follow-up occurring at 2-week intervals (alternating office and telemedicine encounters). The greater time spent with patients allows for attention to adherence (both unintentional and intentional). Unintentional adherence (ie, forgetting to take a medication) can be addressed with education and adherence aids such as pill boxes, phone alarms, and calendars. Intentional adherence (ie, choosing not to take a medication) can be addressed by employing a patient-centered approach to care, incorporating assessments of psychosocial and other patient-specific factors that may influence patient behavior. Although it was not assessed, based on our data, adherence may have played a significant role as the mean number of antihypertensives between baseline and end of study was not statistically different. Additionally, the incorporation of home BP monitoring and telemedicine follow-up likely contributed to a successful intervention. Home BP monitoring allows for more feasible frequent follow-up, avoidance of white coat phenomenon, and decreased likelihood of clinical inertia because additional data points are made available at clinical encounters. Similarly, home BP monitoring increases patient involvement in care and may increase the sense of accountability to pharmacological and non-pharmacological adherence.

Our investigation has several limitations to note. Subject enrollment was slow and many patients declined participation as part of the informed consent process. This may have introduced selection bias in that those who chose to enroll may have represented patients with the greatest likelihood of successful adherence and/or greatest motivation for health improvement. Additionally, the study did not include a control group to allow comparison to standard of care. Incorporation of a control group was difficult due to the informed consent process, the relatively narrow inclusion criteria, and several methodological issues such as the

inability to blind the groups and the use of routine home BP monitoring and telemedicine follow-up. The study duration was short at a mean of around 4 months. Extending the duration of follow-up may have resulted in either a greater or lesser effect of the intervention and may have allowed demonstration of persistence (or lack thereof) of effect. Finally, the multicomponent intervention may not be feasible in all practices; significant financial (home BP monitors) and human (pharmacists) resources were needed for this service.

Our study was able to demonstrate significant clinical improvement in BP with a pharmacist-managed intervention despite the small number of patients enrolled. The study population consists of low-income, medically underserved, primarily black patients with resistant hypertension. This represents a unique cohort in whom this type of collaborative, pharmacist-managed intervention has not been previously studied. An intervention including home BP monitoring and frequent follow-up by pharmacists is likely to result in similar positive outcomes in other similar patient cohorts.

Authors' Note

This project was presented with preliminary data as a research in progress poster at the American College of Clinical Pharmacy annual meeting, October 2012.

Declaration of Conflicting Interests

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