Initial Medication Selection For Treatment Of Hypertension In An Open-Panel HMO

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Background: **During the past 25 years recommendations for treating hypertension have evolved from a stepped-care approach to monotherapy or sequential monotherapy as experience has been gained and new antihypertensive agents have been introduced. In an effort to develop a disease management strategy for hypertension, we investigated the prescribing patterns of initial medication therapy for newly treated hypertensive patients.**

Methods: **We examined paid claims data of an open-panel HMO located in the midwest. Charts from 377 patients with newly treated hypertension from a group of 12,242 hypertensive patients in a health insurance population of 85,066 persons were studied. The type of medication regimen received by patients newly treated for hypertension during an 18-month period was categorized into monotherapy, sequential monotherapy, stepped care, and initial treatment with multiple agents. With monotherapy, the class of medication was also reported. Associations between use of angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, or β-blockers and presence of comorbid conditions were reported.**

Results: **Fifty-five percent of patients received monotherapy, 22 percent received stepped care, and 18 percent received sequential monotherapy. Of those 208 patients receiving monotherapy, 30 percent were prescribed a calcium channel blocker, 22 percent an ACE inhibitor, and 14 percent a β-blocker. No customization of treatment for comorbid conditions was noted.**

Conclusions: **Physicians attempt to treat patients' hypertension with monotherapy. In the majority of cases, they have used either a calcium channel blocker or ACE inhibitor as initial monotherapy. Costs for treating hypertension could be reduced and care improved if thiazide diuretics, a combination of potassium-sparing and thiazide diuretics, or β-blockers were used more frequently as initial monotherapy. (J Am Board Fam Pract 1995; 8:1-6.)**

The pharmacologic treatment of high blood pressure has evolved considerably in recent years. Twenty-five years ago the study by the Veterans Administration on the treatment of hypertension established the effectiveness of diuretic therapy for the treatment of hypertension.[1] The stepped-care approach to drug therapy evolved during the mid-1970s and was recommended as the approach to treating hypertension in the first report of the Joint National Committee on the Detection, Evaluation, and Treatment of Hypertension in 1977 (JNC 1).[2] During the late 1970s, several research studies began to show the effectiveness of nonpharmacologic interventions in the treatment of hypertension, and this aspect of treatment was addressed by the Joint National Committee in its second report in 1980 (JNC 2).[3] Both JNC 1 and JNC 2 reports recommended beginning therapy with a diuretic as the first step and then adding other agents as needed for blood pressure control.[2,3] By the early 1980s the Hypertension, Detection, and Follow-up Program showed that stepped care was better than referral (usual) care in lowering mortality associated with mild hypertension.[4] Since that time numerous clinical trials have demonstrated the efficacy of both diuretics and β-blockers in reducing the morbidity and mortality associated with high blood pressure.[5-7] In 1984 the Joint National Committee for the Detection, Evaluation, and Treatment of High Blood Pressure in its third report (JNC 3) reaffirmed the use of stepped care but added β-blockers as acceptable initial agents.[7]

During the 1980s two new classes of medications, calcium channel blockers and angiotensin-coverting enzyme (ACE) inhibitors, were de-

Submitted, revised, 13 September 1994.

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veloped and tested for the treatment of hypertension. By 1988 these new antihypertensive medications were being recommended as first-step agents for treatment of hypertension because of their effectiveness and also because of concerns regarding the safety of diuretic therapy and the side effects of diuretics and β-blockers.[8-11] In 1988 the Joint National Committee in its fourth report (JNC 4) expanded its list of acceptable first-step pharmacologic agents to include calcium channel blockers and ACE inhibitors in addition to diuretics and β-blockers.[12]

At the same time, opinion was building in support of individualizing drug therapy based on patient demographics, the presence of comorbid conditions, and quality-of-life issues.[10,13] Also, the potential risks of treating patients with multiple medications was becoming more widely understood. As a result, some experts preferred treating hypertension with sequential monotherapy rather than with stepped care.[10] One theoretical model suggested that a response rate of 70 to 80 percent could be obtained by using sequential monotherapy.[13]

The calcium channel blockers and ACE inhibitors lower blood pressure as well as do diuretics and β-blockers.[14,15] These newer antihypertensive agents, however, have not yet been shown to reduce mortality from hypertension.[5,16] As a consequence, the fifth report of the Joint National Committee (JNC 5) in 1993 re-emphasized the use of thiazide diuretics and β-blockers as initial therapy for high blood pressure.[16] The report suggested that the newer antihypertensive medications be used mainly as second-line agents except where special circumstances warrant their use as a first-line agent.

In 1993 John Deere Health Care, in collaboration with Mayo Clinic, began developing a disease management strategy for hypertension. As part of this process, we performed an evaluation of the cost of care for enrollees with high blood pressure, the type of medications they were prescribed, and the presence of coexisting medical conditions. Our ability to access a large body of claims data allowed us to describe these costs, medication profiles, and diagnosis profiles. This paper describes the medications used for initial treatment of hypertension.

Methods

The population for this study was composed of employees and retirees of Deere & Company and their dependents whose primary residence during their most recent employment was Waterloo, Iowa, or the Quad Cities area (Davenport-Bettendorf, Iowa, or Moline-Rock Island, Illinois). To be included, they needed to have been enrolled in John Deere Health Insurance for at least 1 month during the calendar years 1991 or 1992. The study utilized medical and drug claims submitted by these individuals during 1991 and 1992.

Patients were defined as having hypertension if they filed one or more medical claims with hypertension as either the primary or secondary diagnosis during 1991 and 1992. Hypertension was defined by the following Ninth International Classification of Diseases (ICD-9) codes: 362.11, 401–405, 437.2, 440.1, 796.2.

From the group of patients with hypertension, a subgroup of patients with newly prescribed medication was then defined. To capture this subgroup, we selected the hypertensive patients who met the following two criteria:

1. They were enrolled from January through June 1991 but did not receive antihypertensive drug therapy during that 6-month period.
2. They had at least one prescription for an antihypertensive medication filled during the period of July through December 1991 and at least one prescription for an antihypertensive drug filled during the period of October through December 1992.

We generated a profile of each patient's antihypertensive medication use for the 2-year study period. This profile showed dispensing dates, pharmacologic category, and number of days supply of each agent dispensed. Table 1 lists the pharmacologic classes of antihypertensive medications for study purposes.

The profiles of these patients with newly treated hypertension were reviewed and sorted manually into three categories as follows:

1. *Monotherapy.* Patients who were prescribed only a single pharmacologic class of antihypertensive medication during the study period.
2. *Sequential monotherapy.* Patients who were prescribed drugs sequentially from two or more pharmacologic classes during the period.

Table 1. Antihypertensive Medications by Pharmacologic Class.

Class	Drugs
Angiotensin-converting enzyme inhibitors	Benazepril, captopril, enalapril, fosinopril, lisinopril, quinapril, ramipril
β-Blockers	Acebutolol, atenolol, betaxolol, bisoprolol, carteolol, labetalol, metoprolol, nadolol, penbutolol, pindolol, propranolol, sotalol, timolol
α_1-Adrenergic blockers	Doxazosin, prazosin, terazosin
Other peripherally acting antiadrenergics	Alseroxylon, deserpidine, guanadrel, guanethidine, rauwolfia, rescinnamine, reserpine
Centrally acting antiadrenergics	Clonidine, guanabenz, guanfacine, methyldopa
Calcium channel blockers	Amlodipine, diltiazem, felodipine, isradipine, nicardipine, nifedipine, verapamil
Vasodilators	Hydralazine, minoxidil
Loop diuretics	Bumetanide, ethacrynic acid, furosemide
Thiazide and related diuretics	Bendroflumethiazide, benzthiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, quinethazone, trichlormethiazide
Potassium-sparing diuretics	Any agent containing amiloride, spironolactone or triamterene, either alone or in combination with a thiazide diuretic
Antihypertensive combinations	Any dosage form containing antihypertensive medications from two or more of the above categories in a single dosage form

3. *Stepped care.* Patients who were prescribed a drug from a single pharmacologic class but who later had agents from one or more other classes added to their regimen. Patients who commenced in a sequential monotherapy pattern but later were prescribed agents in two drug classes simultaneously were classified as receiving stepped care.

Patients were excluded if they met two criteria: were prescribed a new class of antihypertensive medication in the last month of the study, and the renewal date for the previous medication was not reached within the study period (n=3). In these cases it was not possible to distinguish sequential monotherapy from stepped care.

Patient claims were searched for evidence of individualization of drug therapy based on comorbid conditions. Patients prescribed a calcium channel blocker or a β-blocker had their records reviewed for the diagnosis of ischemic heart disease (ICD-9 codes 410–414). Patients prescribed an ACE inhibitor had their records reviewed for a diagnosis of congestive heart failure (ICD-9 code 428).

Results

The total study population consisted of 85,066 John Deere employees, retirees, and dependents, from which 12,242 were defined as having hypertension. Of these 12,242 hypertensive enrollees, 377 were defined as having their hypertension newly treated with medication. The medication treatment for these 377 patients is presented in Figure 1. During the 2-year period, 208 of these patients (55 percent) were prescribed monotherapy. The most commonly prescribed medications for initial monotherapy were calcium channel blockers (30 percent of patients), ACE inhibitors (22 percent of patients), thiazide diuretics or potassium-sparing diuretics (22 percent of patients), and β-blockers (14 percent of patients). The type of medications used for monotherapy are presented in Figure 2.

Therapy was assessed to determine whether presence of comorbid conditions influenced selection of the initial agent. Of the 65 patients who were prescribed a calcium channel blocker as initial monotherapy, 12 (18 percent) also submitted a claim during the 2-year period with a diagnosis of ischemic heart disease (ICD-9 codes 410–414); the remaining 53 patients did not have a claim with a diagnosis of ischemic heart disease submitted. Of the 29 patients who were treated with a β-blocker as their initial monotherapy, 2 (7 percent) also submitted a claim with a diagnosis of ischemic heart disease (ICD-9 codes 410–414). Of the 45 patients who were prescribed an ACE inhibitor as their initial monotherapy, none submitted a claim with a diagnosis of congestive heart failure (ICD-9 code 428).

Discussion

Hypertension is one of the most common chronic diseases that primary care physicians are called upon to manage. Our data showed that physicians were treating hypertension using monotherapy:

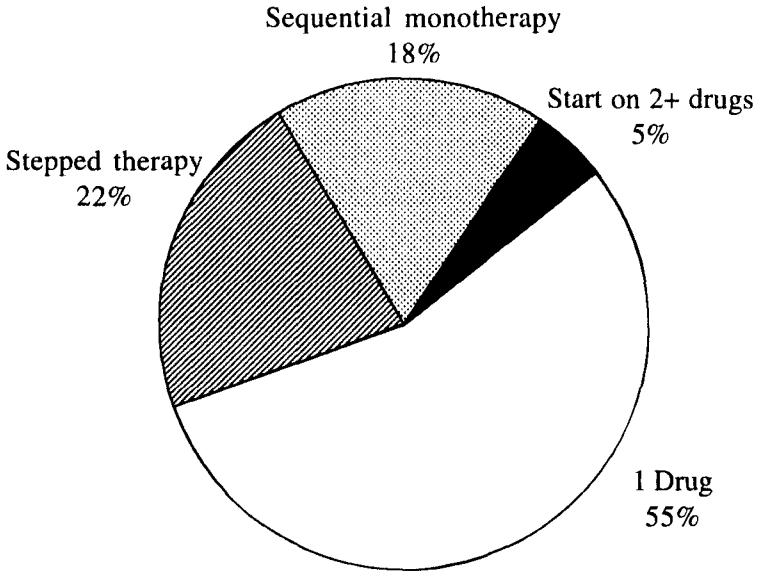

Figure 1. Distribution of initial drug therapy for patients with hypertension (n = 377).

the majority of newly treated subjects received a single drug for the 18-month period. Even though there has been growing interest nationally in using sequential monotherapy, stepped care was the second most common method of treatment. For patients who need a second medication for blood pressure control (stepped care), the Joint National Committee now suggests the physician consider weaning the patient from the first medication once blood pressure control has been achieved with the two-drug regimen.[16] The goal is to simplify therapy to a single medication when possible.

Unfortunately, calcium channel blockers and ACE inhibitors were used more commonly than thiazide diuretics and β-blockers as monotherapy, a finding consistent with the national trends.[5] We initially hypothesized that calcium channel blockers and ACE inhibitors were being prescribed because of preexisting comorbid conditions. The data, however, did not support this hypothesis. The calcium blockers and ACE inhibitors were used regardless of the presence or absence of comorbid conditions. It appears that during 1991 and 1992 these two classes of medication were preferred by clinicians for the initial treatment of hypertension. The reasons for this preference were probably many. In 1988 JNC 4 broadened acceptable initial therapy to include these new antihypertensive agents.[12] During this same period, subgroup analysis of the Multiple Risk Factor Intervention Trial (MRFIT) raised concerns regarding the safety of diuretics.[11] Expert opinion was divided on the best medication to use as initial therapy. Our results suggest that physicians during the 1991–1992 period used a wide variety of agents for initial monotherapy and tended to avoid thiazide diuretics.

JNC 5 now recommends the use of thiazide diuretics and β-blockers as the preferred agents for initial therapy of hypertension.[16] The report states that only these two classes of medications have been shown to reduce mortality from high blood pressure. In addition, a recently released randomized controlled trial comparing these four classes of medication (thiazide diuretics, β-blockers, calcium channel blockers, ACE inhibitors) for the treatment of high blood pressure showed no difference in their rates of adverse drug effects.[14,15] A recent study, however, revived the old concern of excess mortality associated with thiazide diuretic therapy. Siscovick, et al.,[17] in a recent case-control trial, found that potassium-sparing diuretics (triamterene-thiazide) were associated with fewer episodes of cardiac sudden death (arrhythmia complications) than were plain thiazide diuretics or β-blockers. So, a potassium-sparing diuretic might be a better choice than a thiazide diuretic as an initial agent. Even with this caveat, however, it appears that the best care would be to prescribe a diuretic or β-blocker rather than a calcium channel blocker or ACE inhibitor as initial therapy.

Medication costs constitute a considerable portion of the cost of caring for patients with hypertension, with one national study estimating that medication costs represent 36 percent of the ambulatory cost of treating hypertension.[18] The agent chosen for initial drug therapy of high blood pressure has a considerable effect on cost. The average wholesale prices for these medications range from $1.11 for 100 tablets of generic thiazide diuretics and $5.93 for 100 tablets of generic triamterene (75 mg)-hydro-

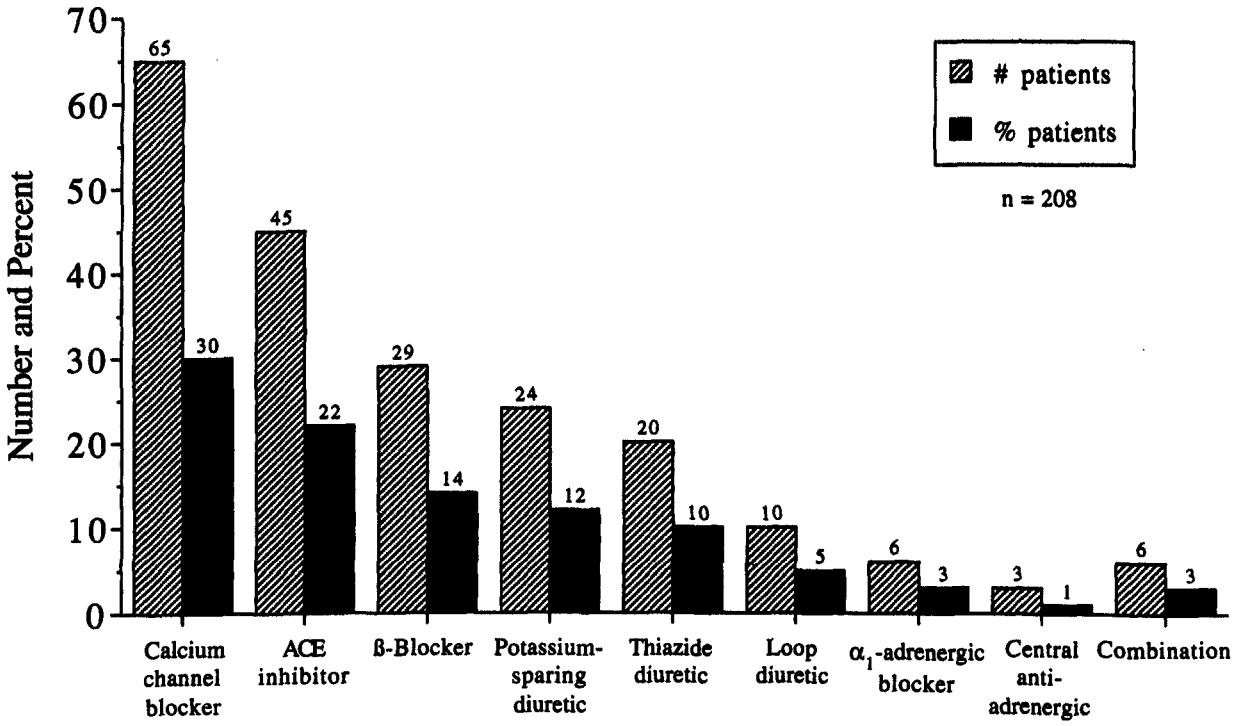

Figure 2. Type of agents prescribed for patients as initial monotherapy (n = 208). ACE = angiotensin-converting enzyme.

chlorothiazide (50 mg) to $103 for 100 tablets of generic verapamil 240-mg sustained release.[19] The use of diuretics or β-blockers as initial therapy of high blood pressure is one instance where the best medical care is not only the most cost-effective but also is less expensive than current treatment patterns.

The challenge is to re-emphasize thiazide diuretics, potassium-sparing and thiazide combination diuretics, or β-blockers as the primary medications for the treatment of hypertension. A number of strategies could be helpful. Traditional continuing medical education activities are one avenue. An avenue available to managed care organizations is to use pharmacy claims information to provide feedback to physicians on their prescribing habits. These data can be presented either as group data, as physician-specific data, or as patient-specific data. Managed care organizations can also work for change through direct physician feedback and by trying to convince local clinical opinion leaders to rethink the treatment of hypertension. Medical groups interested in quality improvement activities could use treatment of hypertension as one of their projects. The important next step will be to recognize the potential this clinical area has for both improved care and lower health care costs.

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