

Treatment of Hypertension in Patients With Comorbidities

Results From the Study of Hypertensive Prescribing Practices (SHyPP)

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Approximately 50 million people have hypertension. Many agents with differing efficacy, side effects, dosing schedules, and costs are available to treat hypertension. Joint National Committee (JNC) guidelines attempt to simplify this decision by recommending specific agents based on special considerations such as comorbidities. The objective of this study was to survey primary care physicians' antihypertensive prescribing practices and their treatment recommendations for patients with comorbidities. A direct mail survey was sent to a national random sample of 500 office-based primary care internists, family practitioners, and general practitioners. There were no significant differences between initial treatment recommendations at the time of the survey and those recommended before the survey. However, there were several therapeutic classes whose reported utilization for specific comorbidities significantly changed over 18 months. Angiotensin converting enzyme (ACE) inhibitors reportedly increased in patients with congestive heart

failure and diabetes. In addition, the reported use of selective β -blockers increased for patients with a history of myocardial infarction. Physicians did not follow JNC recommendations when initiating treatment in black patients, older patients, or those with mild renal failure. Younger physicians were more likely than older physicians to select agents consistent with guideline recommendations. Physicians did not adhere to JNC guidelines when initiating treatment in patients with comorbidities; however, more physicians are prescribing recommended agents today as compared to 18 months ago. Younger physicians were more likely to prescribe agents consistent with the guidelines. More direct efforts are needed to ensure awareness and compliance with these guidelines. Am J Hypertens 1999;12:333-340 © 1999 American Journal of Hypertension, Ltd.

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Hypertension affects approximately 50 million people in the United States.¹ High blood pressure is not only a risk factor for death from cardiovascular causes such as heart attacks, heart failure, and stroke, but also from

kidney failure and blood vessel disease.²⁻⁶ In addition, it is a significant risk factor for coronary heart disease and the most important risk factor for cerebrovascular diseases.¹ With proper treatment, however, this risk can be reduced. In randomized controlled studies of drug treat-

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ment of hypertension, stroke mortality was reduced by one-third, whereas mortality from coronary artery disease was reduced by one-fourth.⁷

Health care providers can choose from many different antihypertensive agents with differing efficacy, side effects, dosing schedules, and costs. The Joint National Committee (JNC) periodically publishes consensus guidelines in an attempt to simplify the decision-making process. The Joint National Committee's fifth report was published in 1993.¹ Previous studies have demonstrated that there is high awareness of JNC recommendations among primary care physicians.⁸ This consensus report reviews antihypertensive treatment recommendations, drug interactions, and adverse effects of various antihypertensive agents. In addition, this report provides recommendations for individualizing initial drug therapy based on special considerations such as comorbidities. Since this report, however, JNC treatment recommendations for patients with coexisting diseases have been further developed by increasing clinical evidence from the literature.⁹ At the time of this survey, JNC-V was the prevailing guideline.

There is limited data in the literature regarding physicians' choice of initial antihypertensive therapy for a patient with concomitant diseases. It is not known whether physicians adhere to JNC guidelines when initiating treatment in patients with comorbidities. To better understand factors that drive physician prescribing, we designed the study of hypertensive prescribing practices (SHyPP). This survey was completed by a national random sample of office-based primary care physicians. Issues assessed in this survey include most frequently prescribed agents, initial treatment recommendations for patients with preexisting comorbidities, and the likelihood of drug interactions for various antihypertensive agents. In light of the recent reevaluation of hypertension treatment guidelines,¹⁰ this survey provides a timely evaluation of primary care physicians' hypertensive prescribing practices.

METHODS

The aim of this survey, which was conducted from May through September 1997, was to determine primary care physicians' perceptions regarding initiation of antihypertensive treatment in patients with comorbidities and drug interactions associated with various classes of agents. This report focuses on select results of the SHyPP study, those that relate to treatment recommendations for patients with comorbidities. Other findings from this study, such as the perceived impact of managed care on prescribing practices and physicians' perceptions about the cost and safety of antihypertensive medications, are reported elsewhere.⁸ Part one of the survey instrument included questions regarding frequently prescribed agents.

Physicians were asked which brand or generic agent within each therapeutic category they prescribed most often.

Part two of the survey focused on initiation of antihypertensive treatment in patients with comorbidities. Physicians were asked which class of agents they would prescribe at present for patients with specific comorbidities as initial therapy for hypertension. In this study, physicians were surveyed only once and were asked to recall how their choices today compared to those 18 months ago.

Part three of the survey determined physicians' perceptions regarding medication risks. Physicians were asked to rank categories of antihypertensive agents in order of their potential for adverse interaction with other medications.

Finally, part four focused on the demographic characteristics of the physicians responding to the survey. Specific questions regarding physician age, ethnicity, gender, medical school graduation year, practice setting, specialty, and patient insurance type were asked.

The survey was mailed with an honorarium to a national random sample of 500 office-based, patient care internists, family practitioners, and general practitioners in March 1997. These physicians were randomly drawn from the American Medical Association's (AMA) masterfile and were not selected on the basis of any other criteria such as their geographic location, practice environment, or the likelihood of treating hypertensive patients. Second and third surveys with honoraria were sent to those physicians who did not respond to the initial mailing. The survey was completed in September 1997. There was no telephone contact with the physicians.

Data Analysis All analyses were based on the number of physicians responding to the question. We analyzed the following: agents most frequently reported to be prescribed, initial treatment recommendations for patients with comorbidities today and 18 months ago, today's treatment recommendations compared across physician age group and specialty, and the perceived likelihood of drug interactions for the various therapeutic agents.

Age groups were defined as ≤ 45 years of age and > 45 years to ensure two groups of comparable size. Physician specialty was classified as internal medicine or family practice. Those physicians reporting their specialty as "other" (3%) were excluded as our analysis was limited to primary care physicians. General practitioners (7%) were also excluded from our analysis as this group was too small to analyze. χ^2 and Fisher's exact analyses were used to test for differences in the distribution of responses for categorical data. McNemar's test, a paired *t* test for categorical data, was used to detect significant differences in

TABLE 1. CHARACTERISTICS OF PRIMARY CARE PHYSICIANS WHO RESPONDED TO SURVEY (n = 268)

Characteristic	
Age (years) mean \pm SD	46.2 \pm 11.5
Gender (%)	
Male	79
Female	21
Ethnic origin (%)	
White	82
Black	4
Hispanic	3
Asian	4
Other	1
No answer	6
Physician specialty (%)	
General internal medicine	43
Family practice	45
General practice	7
Other	3
No answer	3
Practice type (%)	
Single specialty group	42
Multi specialty group	18
Individual physician office	25
Hospital based	7
Other	6
No answer	3
Current practice setting (%)	
Fulltime clinical	85
Parttime clinical	6
Research/teaching/administration	5
Other	3
No answer	3
Patients' insurance, average (%) mean \pm SD	
Fee-for-service	25.9 \pm 20.59
Managed care	34.6 \pm 26.34
Medicare	28.6 \pm 19.69
Medicaid	8.8 \pm 11.02
Other	2.0 \pm 8.54

SD, standard deviation.

Percentages may not add to 100 because of rounding.

paired responses for each comorbidity. Differences for all analyses were regarded as statistically significant if $P < .05$.

RESULTS

Of the 500 primary care physicians to whom the survey was mailed, 268 (53.6%) responded. Table 1 contains demographic information on these respondents. The average age of the physicians was 46.2 years and a majority of the respondents were male, white, and had full-time clinical practice settings.

Agents Most Frequently Prescribed Hydrochlorothiazide was the most frequently reported diuretic

to be prescribed with 61% of physicians reportedly choosing it (Table 2). Atenolol and propranolol were the most frequently reported selective and nonselective β -blockers to be prescribed, whereas lisinopril and enalapril were reported to be the most frequently selected ACE inhibitors. Amlodipine and diltiazem were reported to be the most frequently selected long-acting calcium channel blockers (CCB), whereas 46% of physicians reported not prescribing short-acting CCB at all in their practice.

Antihypertensive Treatment With Comorbidities

There were no significant differences between the overall distribution of responses for initial treatment recommended by physicians at the time of the survey and those recommended 18 months before the survey (Table 3). However, there were therapeutic classes whose reported use for specific comorbidities significantly changed over 18 months, although the changes were modest. The reported use of ACE inhibitors for initial treatment increased in patients with documented congestive heart failure (CHF) and for patients with diabetes at the expense of a significant reduction in the selection of diuretics and long-acting CCB, respectively. Similarly, the reported use of selective β -blockers increased in patients with a history of myocardial infarction (MI) at the expense of long-acting CCB, whereas α -blocker use reportedly increased in patients with hyperlipidemia.

Recommendations by physicians for patients with specific comorbidities are listed in Table 3. For patients with mild renal failure (creatinine level <3 mg/dL), ACE inhibitors and diuretics are recommended for initial treatment, whereas for older patients, diuretics are the recommended treatment.⁹ However, only about one-third of physicians reported initiating treatment with these agents for these groups of patients. Only 8% of physicians reported using diuretics for patients with mild renal failure. For hyperlipidemia, the JNC guidelines state that α -blockers may have favorable effects on lipid profiles, thus they may be beneficial in patients with hyperlipidemia, whereas β -blockers and diuretics can increase cholesterol levels. In our survey, 14% of physicians reported initiating therapy with α -blockers in patients with hyperlipidemia, up from 11% 18 months previous. A comparable number of physicians, however, chose to initiate treatment with β -blockers and diuretics. Similarly, the guidelines recommend not using β -blockers and ACE inhibitors as monotherapy in black patients as these agents may be less effective than other available ones. However, 30% of physicians in our survey reported using these agents as initial treatment and less than half selected a diuretic, which is the recommended agent to be used in this patient population.

There was a statistically significant association be-

TABLE 2. PERCENT OF PHYSICIANS PRESCRIBING AGENTS WITHIN THERAPEUTIC CATEGORIES

Agents	Physicians Prescribing (%)
Diuretics	
HCTZ	61
HCTZ/triamterene	26
Furosemide	7
Bumetanide	<1
Other	9
Do not prescribe	1
Selective BB	
Atenolol	56
Metoprolol	26
Labetalol*	1
Propranolol*	1
Other	6
Do not prescribe	5
Nonselective BB	
Propranolol	54
Metoprolol*	6
Atenolol*	6
Labetalol*	1
Other	6
Do not prescribe	16
ACE inhibitors	
Lisinopril	36
Enalapril	23
Benazepril	13
Fosinopril	8
Quinapril	7
Captopril	7
Ramipril	1
Other	<1
Do not prescribe	1
SA CCB	
Nifedipine	19
Diltiazem	12
Verapamil	9
Nicardipine	<1
Other	1
Do not prescribe	46
LA CCB	
Amlodipine	28
Diltiazem CD, XR, SR	27
Nifedipine XL, CC	18
Verapamil SR	15
Felodipine	2
Nicardipine	<1
Other	7
Do not prescribe	2

CCB, calcium channel blockers; BB, β -blockers; SA, short-acting; LA, long-acting; HCTZ, hydrochlorothiazide.

* Drugs were categorized into classes according to physicians' reported classifications even where incorrect.

tween reported initial treatment and physician age (Table 4). For each category in which an age-specific association was detected, younger physicians were

more likely to select agents consistent with the JNC recommendations. There was no statistical association between physician specialty and initial treatment choices.

Medication Risks A quarter of physicians believed that diuretics were most likely to interact adversely with other medications. Central agents were selected by 20% of physicians and nonselective β -blockers were chosen by 16% as the class of agents most likely to interact adversely with other medications. All other classes of agents were selected by 5% or fewer physicians.

DISCUSSION

In this study, we sought to determine physicians' perceptions of treatment recommendations for patients with hypertension in a comprehensive fashion. This study was motivated by changes in clinical data over the past few years^{1,9,10} and by changes in the practice environment that may be influencing physicians' treatment recommendations. This type of research serves as an assessment of the formal treatment guideline process for hypertension established by the JNC, specifically whether physicians follow consensus recommendations when treating patients with hypertension. Furthermore, in this study, we have focused on the assessment of treatment prescribing practices for patients with comorbidities as data on recommended treatment are most complex for these patients, and have been most influenced by recent treatment studies.⁹

This study demonstrates that physicians do not adhere to JNC guidelines and the clinical evidence that forms the basis of these guidelines when initiating antihypertensive treatment in patients with comorbidities. However, for patients with CHF, diabetes, history of MI, and hyperlipidemia, a greater number of physicians reported to prescribe agents consistent with guideline recommendations today as compared to 18 months previous. In addition, younger physicians were more likely to select recommended agents than older physicians.

For hypertensive patients with CHF, physicians in our survey reported that they increased use of ACE inhibitors for initial therapy. Eighty-two percent of physicians reported using these agents as initial therapy, up from 76% of physicians 18 months previously. In the literature, there has been increasing clinical evidence demonstrating the benefits of ACE inhibitors in heart failure. An overview of randomized trials found that total mortality or hospitalization for patients with congestive heart failure were significantly reduced by ACE inhibitors.¹¹ This reduction was consistent across age, sex, New York Heart Association functional class, and cause of heart failure. The effects

TABLE 3. INITIAL TREATMENT RECOMMENDED BY PHYSICIANS NOW AND 18 MONTHS AGO

	ACE Inhibitors (%)		Diuretics (%)		LA CCB (%)		Selective BB (%)		α -Blockers (%)	
	Now	18 months	Now	18 months	Now	18 months	Now	18 months	Now	18 months
Asthma	38	36	25	26	31	32				
Diabetes (Type I or II)	84	79*			7	10†				
Prior MI	16	15			6	10†	66	60*		
CHF	82	76*	13	17†						
Over 75 years old	29	30	36	37	18	17				
Cognitive problems	40	37	30	31	22	23				
Mild renal failure	39	37	8	8	32	35	9	8		
Young athletes	50	48	14	14	19	21†	8	8		
BPH	8	6							81	80
PVD	18	18	13	15†	46	44			9	8
Renovascular HTN	34	34	6	7	31	29	14	14		
Depression	46	45	21	22	25	25				
Impotence	46	46	17	16	18	19			13	13
Black	20	20	41	43	23	23	9	9		
Hyperlipidemia	43	45	9	9	21	23	9	7	14	11†
PUD	39	40	24	25	19	18	10	9		

BB, β -blockers; LA, long-acting; CCB, calcium channel blockers; MI, myocardial infarction; CHF, congestive heart failure; PVD, peripheral vascular disease; HTN, hypertension; PUD, peptic ulcer disease.

Percents based on the number of physicians responding to "now" and "18 months ago" question.

McNemar's test was used to detect significant differences in paired responses now and 18 months ago for specific agents and comorbidities.

Blanks indicate data not analyzable since <5% ($x < 11$) of physicians responded to the question.

* $P < .01$ for now v 18 months ago.

† $P < .05$ for now v 18 months ago.

of ACE inhibitors were greatest in patients with an ejection fraction <0.25 .¹¹

In addition to CHF, the reported use of ACE inhibitors for hypertensive patients with diabetes also increased. Eighty-four percent of physicians reported using ACE inhibitors as initial therapy for patients with hypertension and diabetes, whereas up to 79% of physicians reported this 18 months previously. Many studies have demonstrated the relationship between ACE inhibitors and diabetic nephropathy. A review of studies found that ACE inhibitors reduced urinary albumin excretion in both type I and type II diabetic patients with microalbuminuria and overt proteinuria.¹² In addition, metaanalyses have shown that the renoprotective effects of ACE inhibitors in diabetic renal disease are superior to other antihypertensive agents in terms of decreasing proteinuria and preserving renal function.^{13,14} Thus, ACE inhibitors are being recommended as the treatment of choice for both type I and type II diabetic patients with microalbuminuria, regardless of the presence of hypertension.¹⁵

For hypertensive patients with a history of MI, physicians in our survey reported an increase in the use of selective β -blockers for initial therapy. Sixty-six percent of physicians reported they initially used selective

β -blockers in these patients, whereas 60% reported this 18 months previously. The reported use of nonselective β -blockers, however, decreased with only 11% of physicians selecting them for initial therapy as compared to 13% 18 months ago. β -blockers, as a therapeutic class, have been proven to reduce mortality in patients after MI.¹⁶ In a metaanalysis, overall mortality from vascular causes was reduced by 19% in patients treated with β -blockers after an MI.¹⁷ The reported increased use of selective β -blockers seen in our study may be explained by the pharmacologic differences between selective and nonselective β -blockers. Because B_1 -specific β -blockers are cardioselective, the adverse effects caused by B_2 blockade, such as bronchodilation, vasodilation, mobilization of glucose and free fatty acids, and exercise intolerance, are lessened.¹⁸ In addition, B_1 selectivity is one of the four ancillary properties of β -blockers that is associated with greater cardiovascular risk reduction.¹⁹ These pharmacologic properties may explain the reported increased use of selective β -blockers in hypertensive patients with a history of MI.

In our survey, physicians reported an increase in the use of α -blockers for hypertensive patients with hyperlipidemia. Eleven percent of physicians reported prescribing these agents 18 months ago, whereas 14%

TABLE 4. INITIAL TREATMENT RECOMMENDED WITH SPECIFIC CONDITIONS TODAY COMPARED ACROSS PHYSICIAN AGE

Condition	Age	ACE (%)	Diur (%)	LA CCB (%)	SA CCB (%)	Selective BB (%)	Nonselective BB (%)	α -Blockers (%)	Other (%)	No (%)	P*
Prior MI	<45	11.0	0	4.4	0	73.5	11.0	0	0	0	.024
	>45	20.0	1.1	9.5	0	54.7	13.7	0	0	1.1	
Over 75 years	<45	25.0	39.0	20.6	3.7	6.6	1.5	2.2	1.5	0	< .001
	>45	37.2	33.0	13.8	3.2	3.2	1.1	7.5	0	1.1	
Mild renal failure	<45	44.0	6.0	32.8	1.5	9.7	1.5	1.5	3.0	0	< .001
	>45	33.7	12.0	27.2	2.2	7.6	3.3	8.7	4.4	1.1	
BPH	<45	4.4	0	2.9	0	0.7	0	88.2	3.7	0	.013
	>45	8.4	5.3	5.3	1.1	2.1	1.1	72.6	3.2	1.1	
Renovasc HTN	<45	31.3	6.9	32.1	0.8	15.3	5.3	2.3	6.1	0	< .001
	>45	39.1	6.5	26.1	1.1	10.9	1.1	4.4	9.8	1.1	

Diur, diuretics; BB, β -blockers; SA, short-acting; LA, long-acting; CCB, calcium channel blockers; other, central agents and other agents; no, physicians who answered 'none' and 'don't know'; MI, myocardial infarction; BPH, benign prostatic hypertrophy; PVD, peripheral vascular disease; Renovasc HTN, renovascular hypertension; PUD, peptic ulcer disease; CHF, congestive heart failure.

* Fisher's exact test was used to detect significant differences in the distribution of responses across physician age group.

reported this today. There is increasing clinical evidence in the literature regarding the benefit of α -blockers in patients with hypertension and high cholesterol levels. In a multicenter, randomized double-blind study, doxazosin decreased total cholesterol, low density lipoprotein (LDL), and triglyceride levels to a greater extent than other antihypertensive classes.²⁰ Another study found that terazosin produced highly significant reductions in blood levels of total cholesterol, triglyceride, and LDL when used as monotherapy.²¹ In addition to these studies, a meta-analysis including more than 400 trials showed that α -blockers beneficially affected total cholesterol, LDL, and triglyceride levels.²² Despite their beneficial use in hyperlipidemia, α -blockers have not been shown to improve left ventricular ejection fraction or reduce mortality in patients with CHF^{23,24} and they have limited value in reducing ventricular arrhythmias in myocardial infarction.²⁵

Physicians in our survey did not follow JNC guidelines in assessing their initial treatment recommendations for patients with comorbidities. Noncompliance with consensus guidelines has previously been documented in the literature.²⁶ Not all physicians believe that consensus guidelines, such as the JNC recommendations, are a step forward for antihypertensive treatment, further promoting noncompliance.²⁷ Other reasons for why JNC recommendations appear to have had little impact on prescribing practices may include lack of dissemination of these recommendations or pharmaceutical marketing pressures that promote alternative treatments.^{26,28} JNC-VI had not been published when this study was completed; however, the treatment recommendations for patients with comorbidities in this report reflect JNC-V and the research

published since those recommendations were established.⁹ Thus, the data that served as the basis for JNC-VI⁹ was available at the time our study was undertaken, although the information had not been compiled as formal recommendations.

An important point to consider is that although physicians' responses may be consistent with JNC recommendations, there is no reassurance that a patient with a particular comorbidity will receive the recommended agent. This disparity may be attributable to reasons such as issues with knowledge of guideline recommendations, physicians' diagnostic skills, or clinical decision-making skills.

Limitations There are some limitations to our study. The sample size used in our survey was small. Both reporting and selection bias are possible in a direct mail survey. We did not have any available data regarding nonrespondents in our survey, thus we were unable to characterize the practices of those who did not respond. Our study assessed self-reported behaviors that may not reflect accurately actual prescribing practices. A previous study documented that there is often a disparity between what physicians report they prescribe and national prescribing practices.⁸ This particular study surveyed a national random sample of office-based primary care physicians and found that reported prescribing choices were not necessarily consistent with true prescribing practices. Future studies regarding prescribing practices could validate physicians' answers against objective measurements such as retrospective or prospective medical chart documentation. Our survey asked about prescribing practices today and 18 months ago at the same point in time, thus physicians' answers regarding initial treatment

choices 18 months ago may be influenced by their current prescribing practices. Because this was a one-time survey, our study could understate differences in prescribing patterns due to recall bias based on current practices.

In this study, some of the comorbidities mentioned are rather broad in nature. Thus, physicians left to their professional judgment and diagnostic ability for interpretation may have defined some of these disease states differently. This, in turn, could lead to greater variability among respondents. Finally, as the nature of our analysis was descriptive, we did not control for type I error when comparing physician prescribing practices now and 18 months ago.

The SHyPP study has documented current trends in perceived antihypertensive prescribing behavior for patients with comorbidities. Physicians in our study did not adhere to the JNC guidelines when initiating antihypertensive treatment in patients with comorbidities. However, for patients with CHF, diabetes, a history of MI, and hyperlipidemia, a greater number of physicians reported to prescribe agents consistent with the JNC guidelines today as compared to 18 months ago. In addition, younger physicians were more likely to select recommended agents than older physicians. Studies such as these demonstrate the need to periodically assess physicians prescribing practices according to comorbidities. Adherence to these clinical practice guidelines will help promote safe and effective pharmacotherapy of hypertension in patients with comorbidities. This study highlights the need for more direct efforts to help ensure awareness and compliance with these recommendations.

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