Trends in Antihypertensive Drug Therapy of Ambulatory Patients by US Office-Based Physicians

Cheryl R. Nelson, Dee A. Knapp

Abstract—This study assessed trends from 1980 to 1995 in ambulatory patients' antihypertensive drug therapy by US office-based physicians for visits in which hypertension was the principal diagnosis and compared these trends with the respective guidelines given in 5 Joint National Committee (JNC) Reports on Detection, Evaluation, and Treatment of High Blood Pressure published around the same time period. Data from the National Center for Health Statistics’ National Ambulatory Medical Care Surveys for 1980, 1985, 1990, and 1995 were used. From 1980 to 1995, there was no significant trend in the percentage of hypertension visits that did not mention any antihypertensive drug (20% to 27%). Further analyses focused on those hypertension visits in which at least 1 antihypertensive drug was used. Across the years, antihypertensive drug visits mentioning calcium channel blockers or ACE inhibitors significantly increased; those noting diuretics significantly decreased. However, in 1995, antihypertensive drug visits that included a diuretic and/or a β-adrenergic blocker equaled 53%; these are the antihypertensive drug classes preferred by the JNC V. Physician antihypertensive drug prescribing was generally consistent with the basic antihypertensive drug guidelines of the JNC reports. (Hypertension. 2000;36:600-603.)

Key Words: antihypertensive agents ■ hypertension, essential ■ drug therapy

Hypertension has been the most frequent principal diagnosis for ambulatory patients by US office-based physicians for more than a decade (National Ambulatory Medical Care Surveys [NAMCS]). In 1995, it accounted for 3.2% of these visits. The purpose of this study was to (1) assess NAMCS trends from 1980 to 1995 in ambulatory patients’ antihypertensive drug therapy by US office-based physicians at visits in which hypertension was the principal diagnosis and (2) compare these trends with the respective guidelines given in the 5 Joint National Committee (JNC) reports published around the same time period. These were 1975 to 1976, JNC I; 1980, JNC II; 1984, JNC III; 1988, JNC IV; and 1993, JNC V. The most recent, JNC VI, was published in 1997.

There have been other national surveys that have evaluated antihypertensive drug prescribing trends. However, NAMCS data have the advantages of methodological and analytical consistencies, coverage of the time periods necessary to measure the effects of the first 5 JNC reports, and the ability to assess antihypertensive drug pattern characteristics during patient visits.

Methods

NAMCS is a national, probability-sample survey conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention. It collects data on medical care services provided by office-based physicians during ambulatory patient visits. To assess a 15-year trend in antihypertensive drug therapy, 1980, 1985, 1990, and 1995 NAMCS data were used. NAMCS medication data were first collected in 1980. Detailed information on NAMCS sampling and data collection is given in other NAMCS references.

Only patient visits having a principal (first-listed) diagnosis of essential hypertension (ICD-9-CM code 401) were included for this study. The JNC reports were used to identify and classify the antihypertensive drugs. To analyze antihypertensive drug prescribing, the following coding procedures were performed. Each hypertension visit in which at least 1 antihypertensive drug was mentioned was counted as an antihypertensive drug visit. On the NAMCS data collection forms, physicians could record the antihypertensive drugs prescribed during the visit by using either generic drug names or brand names. Where brand names were listed, each generic name (active ingredient) component of the drug product was coded separately. Then, each occurrence of an antihypertensive generic name was categorized to its major antihypertensive drug class. If a particular antihypertensive drug class occurred more than once for a visit, it was counted only once. For the first analysis, antihypertensive drug class occurrences, the frequency of occurrence for each antihypertensive drug class across all antihypertensive drug visits was computed. The second analysis focused on antihypertensive drug class patterns. For each antihypertensive drug visit, the pattern of the different antihypertensive drug class(es) prescribed concomitantly was tallied; then, the frequency across all visits associated with each unique pattern was computed.

The standard errors used in tests of significance were calculated by means of generalized linear models for predicting the relative standard error for estimates, based on the linear relation between the actual standard error, as approximated by SUDAAN software, and the size of the estimate.
A weighted least-squares regression method was adapted to analyze selected trends for NAMCS years 1980, 1985, 1990, and 1995. The determination of statistical significance was based on the 2-tailed $z$-test, with a critical value of 1.96 (0.05 level of significance). The determination of statistical differences between estimates used the Bonferroni inequality to establish the critical value (0.05 level of significance), based on a 2-tailed $t$-test.

**Results**

The estimated number and percent of hypertension visits in which at least 1 antihypertensive drug was mentioned were, respectively, 1980, 19,985,000 (79.5%); 1985, 19,770,000 (75.9%); 1990, 20,040,000 (73.4%); and 1995, 17,510,000 (77.6%). There was no significant trend for these percentages.

**Antihypertensive Drug Therapy**

Figure 1 shows the antihypertensive drug class occurrences. With the exception of the $\beta$-adrenergic/$\alpha$B blocker and $\alpha_1$-adrenergic antagonist drug classes, trends for all other antihypertensive drug class occurrences were significant. Calcium channel blocker visits increased from 1.9% in 1985 to 39.8% in 1995; ACE inhibitor/receptor blocker visits increased from 6.4% to 37.0%, respectively. The first ACE inhibitor and calcium channel blocker were approved in the United States in 1981 and 1982, respectively. The remaining antihypertensive drug classes decreased.

For each year, the 5 most frequently occurring antihypertensive drug class patterns are shown in Figure 2. Examples of the interpretation of Figure 2 are as follows: in 1980, 37.9% of antihypertensive drug visits used the diuretic drug class without any other antihypertensive drug classes, whereas 13.6% used centrally acting $\alpha_2$-agonist and diuretic drug classes concomitantly without any other antihypertensive drug classes. Across the years, the number of single-drug class antihypertensive drug patterns among the top 5 patterns increased, from 2 such patterns in 1980 to 3 in 1985 to 4 in 1990 and 1995. From 1980 to 1995, none of the top 5 antihypertensive drug patterns included more than 2 different antihypertensive drug classes used concomitantly. During 1980 to 1995, antihypertensive drug patterns consisting of only 3 different antihypertensive drug classes used concomitantly occurred in $\approx$8.4% of the antihypertensive drug visits (not shown in Figure 2). Of the top 5 antihypertensive drug class patterns that occurred throughout 1980 to 1995, only one pattern had a significant trend: Diuretics alone were prescribed during 11.6% of antihypertensive drug visits in 1995, a significant decline from the 37.9% use in 1980. On the basis of percentage of antihypertensive drug visits, diuretics and $\beta$-adrenergic/$\alpha$B blockers, either alone or concomitantly with other antihypertensive drug classes, dominated the top 5 antihypertensive drug class patterns across the years, except for 1995. Survey year 1990 marked the first occurrence of the ACE inhibitor/receptor blocker and calcium channel blocker antihypertensive drug classes among the top 5 patterns, and in 1995 they led the prescribing patterns.
First Two Recommended Pharmacological Treatment Steps by Major Antihypertensive Drug Class: JNC I–V

<table>
<thead>
<tr>
<th>JNC (Publication Year)</th>
<th>Step 1 Drug Class(es)* (No. of US-Approved Active Ingredients, by Class)</th>
<th>Step 2 Drug Classes* (No. of US-Approved Active Ingredients, by Class)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (1977) and II (1980)</td>
<td>Diuretic (16)</td>
<td>Add: α_{1}-adrenergic antagonist (1) or β-adrenergic blocker (3) or centrally acting α_{2}-agonist (2) or peripherally acting antihypertensive agent (5)</td>
</tr>
<tr>
<td>III (1984)</td>
<td>β-adrenergic blocker (8) or diuretic (19)</td>
<td>Add: Step 1 drug class not already used or ACE inhibitor (1) or α_{1}-adrenergic antagonist (1) or calcium channel blocker (3) or centrally acting α_{2}-agonist (3) or peripherally acting antihypertensive agent (6)</td>
</tr>
<tr>
<td>IV (1988)</td>
<td>ACE inhibitor (3) or β-adrenergic blocker (9) or calcium channel blocker (4) or diuretic (19)</td>
<td>Add: Step 1 drug class not already used or α_{1}-adrenergic antagonist (1) or centrally acting α_{2}-agonist (4) or direct vasodilator (2) or peripherally acting antihypertensive agent (6)</td>
</tr>
<tr>
<td>V (1993)</td>
<td>ACE inhibitor (7) or α_{1}-adrenergic antagonist (3) or β-adrenergic blocker (9) or diuretic (17)</td>
<td>Add: Step 1 drug class not already used or centrally acting α_{2}-agonist (4) or direct vasodilator (2) or peripherally acting antihypertensive agent (6)</td>
</tr>
</tbody>
</table>

From References 2 through 6.  
Example: JNC I-II recommended the diuretic class as the step 1 antihypertensive drug class. If there was an inadequate response, then the recommendation was to add one of the following classes: α_{1}-adrenergic antagonist or β-adrenergic blocker or centrally acting α_{2}-agonist or peripherally acting antihypertensive agent. Within the diuretic class, there were 16 active ingredients (generic drug names) approved in the United States by 1980.  
*Antihypertensive drug class names for each JNC step are presented in alphabetical order, not preferential order.  
†JNC V preferred step 1 antihypertensive drug class.

Figure 3 focuses on the relations of the diuretic and β-adrenergic/αβ blocker drug class patterns versus the ACE inhibitor/receptor blocker and calcium channel blocker drug class patterns between 1990 and 1995. In 1990 and 1995, those antihypertensive drug visits that included a diuretic and/or a β-adrenergic/αβ blocker were significantly greater than those antihypertensive drug visits that included an ACE inhibitor/receptor blocker and/or a calcium channel blocker (but without a diuretic and/or a β-adrenergic/αβ blocker): 1990, 60.5% versus 31.2%; 1995, 53.1% versus 43.9%. This occurred even though the β-adrenergic/αβ blocker and/or diuretic visits significantly decreased from 1990 to 1995 (60.5% to 53.1%), whereas the calcium channel blocker and/or ACE inhibitor/receptor blocker visits (without β-adrenergic/αβ blockers and/or diuretics) significantly increased (31.2% to 43.9%).

JNC Report Comparisons
JNC I (1975 to 1976) and JNC II (1980) recommendations were compared with the 1980 NAMCS, JNC III (1984) with the 1985 NAMCS, JNC IV (1988) with the 1990 NAMCS, and JNC V (1993) with the 1995 NAMCS. The Table abstracts the recommended initial antihypertensive drug treatments of JNC I-V.

The 1985 NAMCS (Figure 2) showed prescribing patterns were generally consistent with 1984 JNC III guidelines. The used-alone patterns of the diuretics and β-adrenergic blockers accounted for 42.2% of the antihypertensive drug visits. β-adrenergic blockers used alone increased from 6.3% of the antihypertensive drug visits in 1980 to 14.8% in 1985. Visits involving (1) only β-adrenergic blockers and diuretics concomitantly and (2) only centrally acting α_{2}-agonists and diuretics concomitantly were 24.0% of the antihypertensive drug visits; both of these patterns were acceptable JNC III step 2 approaches. Of the antihypertensive drug visits, 5.3% used centrally acting α_{1}-agonists alone; JNC III noted that under certain unspecified conditions this drug class could be appropriate for step 1 drug therapy.

The 1990 NAMCS (Figure 2) showed that prescribing patterns were consistent with the 1988 JNC IV guidelines. Four of the top 5 antihypertensive drug patterns were step 1 drug classes used alone, with the remaining pattern using a step 2 recommendation of using 2 step 1 drug classes concomitantly.

The 1995 NAMCS (Figure 2) showed that the basic 1993 JNC V pharmacological guidelines were followed. Four of the top 5 antihypertensive drug patterns were single step 1 drug classes. The remaining pattern used the diuretic class concomitantly with another step 1 drug class (ACE inhibitor). Of the top 5 antihypertensive drug class patterns, the JNC V’s preferred step 1 monotherapy of either diuretics or β-adrenergic blockers comprised together 19.6% of the antihypertensive drug visits, whereas the monotherapy of either calcium channel blockers or ACE inhibitors comprised together 39.5% of the antihypertensive drug visits. However, as noted in Figure 3, patterns that included diuretics and/or β-adrenergic blockers accounted for 53.1% of the antihypertensive drug visits.

Discussion
From 1980 to 1995, 20.5% to 26.6% of hypertension visits had no mention of antihypertensive drug therapy. How much of this was true nonantihypertensive drug prescribing versus...
item nonresponse is not known. An unknown portion of true nonantihypertensive drug prescribing could have been for those cases in which nonpharmacological treatment (lifestyle modification) alone was being used.

An aforementioned study 10 found a decline in diuretic and β-blocker dispensed prescriptions and an increase in calcium antagonist and ACE inhibitor dispensed prescriptions between 1992 and 1995. Our study (Figure 2) noted a similar decrease in monotherapy in which JNC V’s preferred drug classes of diuretics or β-adrenergic blockers were used (monotherapy visits of these two classes together equalled 44.2% of antihypertensive drug visits in 1980 versus 19.6% in 1995). However, in 1995, Figure 3 showed visits including a diuretic and/or β-adrenergic blocker were prescribed in 53.1% of antihypertensive drug visits. Thus, the two preferred antihypertensive drug classes were still prescribed in a little more than half of the antihypertensive drug visits but usually not as monotherapy (53.1% minus 19.6% monotherapy equals 33.5%). Since NAMCS does not ascertain medication history, it was not known in what temporal order the antihypertensive drugs were prescribed for those visits involving 2 or more antihypertensive drugs. In summary, from 1980 to 1995, physician antihypertensive drug prescribing was generally consistent with the basic antihypertensive drug guidelines of JNC I-V. However, NAMCS does not contain the information that could impute the amount of causality attributable to the JNC reports on these trends.

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References
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