

ANTIHYPERTENSIVE DRUGS USED BY HYPERTENSIVE PATIENTS IN THE PROVINCIAL CITIES OF ISFAHAN, NAJAFABAD AND ARAK

AR Khosravi⁽¹⁾, Sh Shirani⁽²⁾, Sh Shahrokhi⁽³⁾
N Mohammadifard⁽⁴⁾, R Ansari⁽⁵⁾

Abstract

INTRODUCTION: Hypertension is the most prevalent chronic disease encountered by physicians. Its prevalence has been reported at 18% in Isfahan province. Hypertension control decreases the risk of stroke and coronary events by 50% and 15%, respectively. According to the World Health Organization (WHO), the rate of blood pressure control stands at 12.5%. Effective hypertension control requires measures such as screening, diagnosis, lifestyle improvement, and drug therapy. The type of drug regimen prescribed to the hypertensive patient is of key importance in achieving optimal control. The present study was performed to determine the type of drugs used by hypertensive patients in urban and rural areas of the provincial cities of Isfahan, Najaf-Abad and Arak.

METHODS: This descriptive cross-sectional study was performed in the provincial cities of Isfahan, Najaf-Abad and Arak in 2000-2001, as part of Isfahan Healthy Heart Program (IHHP). Cluster sampling method was used to select 10674 individuals from the urban and rural areas of the said provincial cities. The patients had systolic blood pressure greater than 140 mmHg, or diastolic blood pressure greater than 90 mmHg or both, or received antihypertensive medications. Data were entered into the EPI-5 software and analyzed with t-test using SPSS.

RESULTS: A total of 2015 hypertensive individuals (18.9%) were identified. Awareness of being hypertensive and rate of treatment and control of hypertension measured 47%, 23% and 9% respectively. Of 670 patients under treatment, 527 had been treated with one drug type, 133 with two drug types with 35 different combinations, and 30 used three drug types with 25 different combinations. Among single-drug regimens, beta-blockers were the most common choice (23%) and atenolol and methyldopa were the most frequently prescribed drugs, respectively. The frequency of diuretics use was 0.9%. Inappropriate combinations such as atenolol plus propranolol were seen among two- and three-drug regimens (nine patients).

DISCUSSION: Drug regimens used by many hypertensive patients are not consistent with standard protocols; these regimens are ineffective in blood pressure control and lead to increased side-effects and subsequently patient noncompliance. Thus, further education of physicians and other healthcare providers on hypertension and antihypertensive treatment seems essential.

Keywords • Hypertension • Adults • Antihypertensive drugs • Combinational regimens

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Introduction

Hypertension is the most common chronic disease treated by physicians.¹ Fifty-eight million Americans are known to be hypertensive.² Studies in the Iranian provincial cities of Tehran and Isfahan have estimated the prevalence

of hypertension in these cities to be nearly 18%.³ Several studies have demonstrated the link between hypertension and cardiovascular diseases.⁴ Treatment of hypertension decreases cerebrovascular accidents (strokes) and coronary artery disease by nearly 50% and 20%, respectively.^{4,6}

(1) Alireza Khosravi MD. Assistant Professor, Cardiologist, Clinical Studies Dept. Isfahan Cardiovascular Research Center, PO. Box: 8146-1148. Email: a_khosravi@crc.mui.ac.ir

(2) Shahin Shirani MD. Assistant Professor. Cardiologist, Isfahan University of Medical Sciences.

(3) Shahnaz Shahrokhi MD. Social Medicine. Isfahan Cardiovascular Research Center.

(4) Nooshin Mohammadifard M.Sc. Research Assistant. Nutritional Research Department, Isfahan Cardiovascular Research Center.

(5) Rezvan Ansari, Research Assistant, Isfahan Cardiovascular Research Center

Corresponding author: Alireza Khosravi MD.

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Previous studies have estimated the control rate of hypertension in Isfahan at 18%.²

Several reasons have been cited for lack of hypertension control, including unawareness of being hypertensive, failing to use medications, irregular use of medications, using medications at inadequate doses, and using the wrong drug combinations. The type and correct combination of antihypertensive drugs are central to achieving better control rates. Today, many types of antihypertensive drugs are available; besides controlling blood pressure, correct use of these drugs contributes to longevity and reduced patient mortality rates.⁷ Diuretics (thiazide drugs in particular) and beta-blockers have been suggested by many studies as the first drugs of choice in treating hypertension owing to their recognized role in reducing cardiovascular mortality and morbidity.^{7,8,10} The effect of newer drugs in reducing cardiovascular mortality and morbidity has also been studied. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNCVII) has recommended the use of a diuretic or a beta-blocker as the first treatment of choice (if not contraindicated) for hypertension.⁸ Using the long-acting forms of calcium antagonists and stopping the use of short-acting forms of nifedipine, especially in coronary artery disease patients has been recommended.⁹ Combination therapy using small drug doses is among other recommended methods, which improve the effectiveness and reduce the complications compared to when high doses of a single drug are used.¹⁰ Assessment of the type of drugs administered to hypertensive patients and making necessary adjustments is essential to achieving better hypertension control. An American study found that 55% of hypertensive patients were on single-drug regimens, whereas first-line drugs (diuretics) had been initiated only in 30% of the cases and calcium antagonists were the most commonly prescribed drugs at the start of treatment.¹² However, hypertension control rates in the US are significantly higher than in Iran. Hypertension control rates in the US and Iran have been reported at 32% and 8%, respectively. Hypertension is a major health challenge in Iran; hence assessment and adjustment of the drug regimens used to treat this condition are essential to achieving better control rates, reducing complications and contributing to longevity in hypertensive patients. The present study was conducted to evaluate the common antihypertensive drug combinations

prescribed to patients in the provincial Iranian cities of Isfahan, Najaf-Abad and Arak.

Materials and methods

This descriptive-cross sectional study was performed in 2000-2001 in three Iranian provincial cities of Isfahan, Najaf-Abad and Arak, which are the areas studied by the pilot national program for the prevention of cardiovascular diseases and stroke, Isfahan Healthy Heart Program (IHHP).

Sampling was performed in each provincial city (consisting of the city and villages in its vicinity) using the randomized cluster sampling method. Cluster sampling in Isfahan was conducted at 15 polio vaccination posts set up across the city (1996). Cluster sampling in Arak was also conducted at polio vaccination posts where 10 clusters were selected. In the city and villages of Najaf-Abad, as well as in villages of the provincial cities of Isfahan and Arak, clustering was conducted at Health and Treatment Centers in these areas. Seven clusters from the city of Najaf-Abad, as well as 8, 7 and 13 clusters from the villages of Najaf-Abad, Isfahan and Arak were selected, respectively. One out of every ten households in each cluster was selected. In every household, one individual from the age groups of 19-24, 25-34, 35-44, 45-54, 55-64, or above 65 years was randomly selected. The sample size in all three provincial cities was calculated at 12600 individuals. Considering the pattern of population distribution in urban and rural areas and the age distribution of the population, equal numbers of male and female subjects were selected. A written questionnaire was completed for each of the subjects by a trained interviewer. The questionnaire was designed to collect demographic information. The subjects were asked to present to day clinic where a questionnaire on hypertension history and antihypertensive treatment would be completed for them. Under identical conditions and according to standard protocol, the subjects' blood pressure was measured by a qualified nurse after at least five minutes of resting in sitting position. Measurement was conducted with a sphygmomanometer on both hands. The highest pressure reading was recorded.

Korotkov's sounds 1 and 5 were considered as systolic and diastolic blood pressure, respectively. Two measurements were performed five minutes apart and the mean of two measurements was recorded as the patient's first blood pressure reading.

Subjects with systolic pressure greater than 140 mmHg, or diastolic pressure greater than 90 mmHg or both, who did not receive antihypertensive medications were asked to present to clinic for a second time. Blood pressure measurement was conducted by the same nurse using the same method and the mean of the first and second measurements was recorded as the individual's blood pressure.

Subjects with systolic blood pressure greater than 140 mmHg, or diastolic pressure greater than 90 mmHg or both, and those receiving antihypertensive medications within at least 7 days of entering the study were considered as hypertensive.

Subjects with hepatic, renal or hematological disease and pregnant women were excluded from the study. Data were entered into EPI-5 software and statistically analyzed with SPSS.

Results

A total of 10679 individuals, comprising 84% of IHHP subjects were studied. Table 1 represents sex and age distribution of subjects. Of the entire population studied, 1015 individuals were hypertensive. The overall prevalence of hypertension in all three provincial cities measured 18.9%, i.e. 1092 women (19.6%) and 923 men (18.1%). Table 2 shows the prevalence of hypertension according to sex and age. Table 3 shows mean systolic and diastolic blood pressure in men and women according to age.

Systolic and diastolic blood pressure in men was higher than in women (P=0.000). Of all hypertensive individuals, 952 (47%) were aware of their condition;

670 (33%) of these were under treatment and only 181 (9%) had controlled blood pressure (blood pressure below 140 mmHg/90 mmHg).

Six-hundred-seventy hypertensive patients were on antihypertensive medications; 459 (69%) of these were women and 211 (31%) were men.

Five-hundred-twenty-seven (77%) patients, including 367 women (72%) and 160 men (28%) were on single-drug regimens.

Table 4 shows the frequency of antihypertensive drugs prescribed to patients on single-drug regimens.

Of the patients under treatment, 113 (17%) including 76 women (11%) and 37 men (5%) were on two-drug regimens with 35 different combinations.

Table 5 shows the frequency of different combinations in two-drug regimens. Thirty patients were on three-drug regimens with 25 different drug combinations.

Inappropriate combinations such as atenolol plus propranolol, or an angiotensin converting enzyme (ACE) inhibitor plus a potassium-sparing diuretic were also seen.

Discussion

Hypertension is the commonest cardiovascular disease and one of the major causes of patient mortality and morbidity.^{12,13} Correct treatment and prescription of appropriate antihypertensive drugs are essential to achieving optimal control.

The prevalence of hypertension in this study measured 18.9% (18.1% in men, 19.6% in women).

TABLE 1. Age and sex distribution of individuals in the provincial cities of Isfahan, Najaf-Abad and Arak

Age (years)	Women	Men	Total
<20	168	200	368
20-29	1542	1445	2987
30-39	1625	1296	2921
40-49	993	892	1885
50-59	566	575	1141
60-69	494	458	952
≤70	185	240	425
Total	5573	5106	10679

TABLE 2. Comparison of the distribution of hypertension in men and women according to age in the provincial cities of Isfahan, Najaf-Abad and Arak

Age (years)	Women, N (%)	Men, N (%)	P value	Total, N (%)
<20	3(1.8)	12(6)	0.00	15(4.1)
20-29	58(3.8)	92(6.4)	0.00	105(3.5)
30-39	138(8.5)	118(9.1)	0.01	256(8.8)
40-49	245(24.6)	168(18.8)	0.00	413(21.9)
50-59	249(44)	188(32.7)	0.00	437(38.3)
60-69	282(57.1)	210(45.9)	0.00	492(51.7)
≤ 70	117(63.2)	135(56.3)	0.00	252(59.3)
Total	1092(19.6)	923(18.1)	0.00	2015(18.9)

TABLE 3. Comparison of mean systolic and diastolic blood pressure in men and women according to age in the provincial cities of Isfahan, Najaf-Abad and Arak

Age (year)	Systolic blood pressure			
	Women Mean±SD**	Men Mean±SD	P value	Total Mean±SD
<20	103.6±13.6	110.7±14.7	0.000	107.5±14.6
20-29	106±13.7	111.7±13.1	0.000	108±13.7
30-39	109.7±15.2	119.1±13.4	0.02	110.7±14.5
40-49	118.9±20.2	117±16	0.000	118±18.4
50-59	129.7±22.4	124.5±20.4	0.000	127.1±21.6
60-69	136.6±22.9	132.4±22.6	0.005	134.6±22.8
70≤	135.7±21.9	138.1±25.7	0.3	137.1±23.2
Total	115.4±20.6	117.2±18.3	0.000	116.2±19.6

*SD: Standard Deviation

TABLE 4. Frequency of antihypertensive drugs of choice in single-drug regimens according to sex in the provincial cities of Isfahan, Najaf-Abad and Arak

Age (year)	Diastolic pressure			
	Women Mean±SD*	Men Mean±SD	P value	Total Mean±SD
<20	69.2±9.2	72.1±9.4	0.000	70.8±9.4
20-29	70.5±9.7	72.9±9.1	0.000	71.7±9.5
30-39	73.1±10	74.2±10.1	0.003	73.6±10.1
40-49	77.8±12.4	77.1±10.2	0.2	77.5±11.4
50-59	82.8±12.9	80.2±11.6	0.000	81.5±12.3
60-69	83.6±12	81.7±11.9	0.02	82.7±12
≤ 70	83.2±12.8	82.5±12.6	0.5	82.8±12.6
Total	75.4±12	76±10.8	0.000	76.7±11.4

*SD: Standard Deviation

TABLE 5. Frequency of combinations in two-drug regimens in the provincial cities of Isfahan, Najaf-Abad and Arak

Drug type	Women, N (%)	Men, N (%)	Total, N (%)
<i>Beta-blockers</i>			
Propranolol	23(6.3)	16(10)	39(7.4)
Atenolol	193(52.6)	78(48.8)	271(51.4)
<i>Calcium antagonists</i>			
Nifedipine	15(4.1)	11(6.9)	26(4.9)
Diltiazem	3(0.8)	21(1.3)	5(0.9)
Verapamil	1(0.3)	1(0.6)	2(0.4)
<i>ACE Inhibitors</i>			
Captopril	3(0.8)	2(1.3)	5(0.9)
Enalapril	12(3.3)	4(2.5)	16(3)
<i>Diuretics</i>			
Triamterene H	13(3.5)	8(5)	21(4)
Thiazides			0.9
<i>Alpha-blocker: Prazosin</i>			
Methyldopa	3(0.8)	1(0.6)	4(0.8)
<i>Vasodilator: Hydralazine</i>			
	98(26.7)	37(23.1)	135(25.6)
	3(0.8)	-	3(0.6)
Total	367	160	527

Earlier studies based on previous diagnostic and therapeutic protocols (defining blood pressure levels higher than 160 mmHg/90 mmHg as hypertension) measured the prevalence of the condition in men,

women and the general population at 16.8%, 19.4% and 18%, respectively.³ These studies found the prevalence of hypertension to be higher in men below 40, and women beyond this age.

In this study, awareness of being hypertensive and rate of treatment and control of hypertension measured 47%, 23% and 9% respectively.

Inappropriate drug combinations were found to be highly prevalent.

Diagnostic and therapeutic guides and protocols on hypertension treatment were available at the time of the study, and the drugs of choice and appropriate single-drug and multi-drug regimens were well recognized.^{8,14}

Other studies^{14,16} found nearly 50% of hypertensive patients to be aware of their condition; less than 50% of these patients (25% of total) were receiving treatment and less than half of these patients had it controlled. Otherwise stated, nearly 12.5% of all hypertensive patients had controlled blood pressure.

Another study conducted in Isfahan³ measured awareness of being hypertensive, rate of treatment and control at 47.1%, 23% and 9%, respectively.

These figures are in greater agreement with earlier studies,^{14,16} suggesting lack of improvement in the control rate of hypertension.

Mean systolic and diastolic blood pressure increased with age both in men and women. This can be explained by vascular changes with aging.³

The World Health Organization (WHO) and the World Hypertension League (WHL) have recommended the use of a diuretic or a beta-blocker as the first line of treatment for hypertension.^{11,14}

A US study found only 55% of hypertensive patients to be on single-drug regimens with only 30% taking diuretics as the first line of treatment. Calcium antagonists and ACE inhibitors were found to be the commonest first-line drugs, respectively.¹¹

Another cohort study found diuretics to be used as the first line of treatment in 55% of the cases.

Calcium antagonists and ACE inhibitors were used as the second and third drugs of choice, respectively.¹⁹

The choice of calcium antagonists in the latter study may be due to the higher mean age of patients and the diagnosis of hypertension in old age.

Six-hundred-seventy hypertensive patients were on antihypertensive medications and 527 (77%) were on single-drug regimens. Beta-blockers were the most frequently used first-line medications (~23% of cases).

Atenolol and methyldopa were the commonest prescriptions, respectively. Diuretics accounted for only 0.9% of prescriptions. The said pattern of antihypertensive prescription is not entirely in

agreement with recommended single-drug regimens consisting of a diuretic or a beta-blocker.

Methyldopa is widely prescribed to patients (28%), whereas it is only the first drug of choice in preeclampsia and high blood pressure during pregnancy;¹⁸ this may be due to availability, low price, and limited side-effects of the drug at low doses. The physicians' tendency to prescribe methyldopa may emanate from the fact that it is well tolerated by many patients. The frequency of diuretics prescription (especially thiazide agents) as the first drugs of choice was low (0.9%).

Single-drug regimens consisting of direct vasodilators such as hydralazine have not been recommended; hydralazine has been recommended in combination with beta-blockers or calcium antagonists (diltiazem or verapamil).

It was found in this study that nearly 0.5% of patients received hydralazine as the only antihypertensive treatment. Calcium antagonists available in Iran are of the short-acting type and their use is not recommended in hypertension treatment. Short-acting nifedipine has been excluded from the list of antihypertensive drugs owing to a range of reported side-effects.⁹ However, 4.9% of patients in this study were found to receive nifedipine as the only antihypertensive medicine, a problem which needs addressing. Another recommended method of treating hypertension is combination therapy using small doses of different drug types; this tends to increase the effectiveness of treatment and reduce side-effects compared to single-drug regimens.¹³

WHO and WHL have recommended combinations such as diuretics plus beta blockers, thiazides plus ACE inhibitors, and beta-blockers plus hydralazine, while ruling out combinations such as potassium-sparing diuretics plus ACE inhibitors, beta-blockers plus verapamil and beta-blockers plus diltiazem as inappropriate.¹⁴

In this study, 113 patients including 76 women and 37 men received two-drug regimens with 35 different combinations; the commonest combinations were those of a beta-blocker plus another antihypertensive drug (a recommended combination) (Table 5), and an ACE inhibitor plus another antihypertensive drug, respectively.

Among inappropriate combinations mention can be made of triamterene H plus ACE inhibitors, atenolol plus propranolol, and beta-blockers plus diltiazem, which increase drug side-effects in patients.

Thirty patients received three-drug regimens with nearly 25 different combinations, including inappropriate combinations such as diltiazem plus beta-blockers plus ACE inhibitors, atenolol plus propranolol plus triamterene H, and ACE inhibitors plus triamterene H plus beta-blockers.

In short, the hypertensive patients were found to receive several inappropriate single-drug or multi-drug regimens; this may have been due to the treating physicians' lack of knowledge or the patients' attempted self-therapy. Such therapies not only tend to increase side-effects, but also reduce the beneficial effects of other drugs in decreasing cardiovascular mortality and morbidity.

We recommend improvements to the physicians' training programs on antihypertensive therapy, as well as better education of patients and their associates. We also recommend that long-acting calcium antagonists be made available in Iran.

This study dealt with drugs used by the patients; inappropriate therapies cannot be wholly linked to physicians, as patient noncompliance and self-therapy attempts are an irrefutable reality. This issue remains to be more closely addressed in future studies.

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