

PHYSICIAN ADHERENCE TO HYPERTENSION GUIDELINES IN ANKARA

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ABSTRACT

• **Objective:** Hypertension is an independent risk factor for cardiovascular disease. Clinical trials have documented that antihypertensive therapy reduces cardiovascular complications in hypertensive individuals. Although the awareness of high blood pressure has improved, the percentage of patients whose blood pressure is controlled has remained unchanged. In this study, we evaluated the adherence of physician to hypertension guidelines.

• **Material and Method:** Clinical and demographic characteristics of 711 patients were collected in Ankara, Turkey. A self-reported medical history related to past history of hypertension, diabetes, hyperlipidemia, coronary artery disease, coronary artery by-pass graft operation and cerebrovascular accident was obtained. Medications used regularly for the control of hypertension during two months preceding the interview and classes of prescribed antihypertensive drugs were recorded. Prescription records for hypertension medications were obtained from Intercontinental Marketing Services (IMS)-Health Turkey between 2000-2005.

• **Results:** As a first line antihypertensive therapy, (Angiotensin Receptor Blocker) ARBs are ranked first (33.5%), (Angiotensin Converting Enzyme Inhibitor) ACEI ranked second (21.2%), and followed by beta-blockers (14.1%), and calcium canal blockers (CCB) (12.8%).

According to the IMS-Health data, ACEI were the most common prescribed, and beta blockers were the second, CCB were the third and ARB were the fourth common prescribed antihypertensive drug in Turkey in 2005. One hundred forty four diabetic patients (55%) were using ACEI or ARB and 29 (14%) were using beta blockers as a first line antihypertensive therapy. 60.9% of the patients were using more than one antihypertensive drug.

• **Conclusion:** Our results showed that despite wide declaration, international guidelines have had limited effect on changing physician behavior. We need to be more careful in achieving antihypertensive therapy in accordance with hypertension guideline.

• **Key Words:** Hypertension, antihypertensive drugs, hypertension guidelines. *Nobel Med* 2010; 6(1): 20-25

ANKARA BÖLGESİNDEKİ DOKTORLARIN HİPERTANSİYON KILAVUZLARINA UYUMLARI

ÖZET

• **Amaç:** Hipertansiyon kardiyovasküler hastalıklarda bağımsız bir risk faktörüdür. Klinik çalışmalarda hipertansif kişilerde antihipertansif tedavinin kardiyovasküler komplikasyonları azalttığı gösterilmiştir. Hastalarda yüksek kan basıncı farkında olma oranının artmasına karşın, kan basıncı kontrol altında olan hasta oranı değişmemiştir. Bu çalışmamızda doktorların hipertansiyon kılavuzlarına olan uyumlarını değerlendirmeyi amaçladık.

• **Materyal ve Metod:** Ankara ve çevresinde yaşayan 711 hastanın klinik ve demografik özellikleri kayıt edildi. Hastaların hipertansiyon, diyabet, hiperlipidemi, koroner arter hastalığı, koroner bypass operasyonu ve serebrovasküler hastalıklarla ilgili ilaç kullanım hikayeleri kayıt edildi. Anket yapılmadan iki ay öncesinden itibaren hastaların kullanmakta oldukları antihipertansif ilaçlar ve sınıfları kaydedildi. 2000-2005 yılları arasında Türkiye'de yazılan hipertansiyon ilaç miktarları ve toplam giderleri IMS-Health Turkey kayıtlarından elde edildi.

• **Bulgular:** İlk seçenek antihipertansif tedavide, ilk sırada %33,5 ile angiotensin reseptör blokerleri (ARB), ikinci sırada %21,2 ile angiotensin dönüştürücü enzim inhibitörleri (ACEI) yer almaktadır. Bunları %14,1 ile beta bloker ve %12,8 ile kalsiyum kanal blokeri takip etmektedir. IMS 'den elde edilen 2005 yılı Türkiye genelinde yazılan antihipertansif ilaç verilerine göre, ACEI en sık yazılan ilaç grubu iken, ikinci sırada beta bloker, üçüncü sırada kalsiyum kanal blokeri, dördüncü sırada ARB gelmektedir. Diyabet hastalarının 114'ü (%55) ilk seçenek antihipertansif ilaç olarak ACEI ve ARB ve 29'u (%14) beta bloker tedavi kullanıyordu. Hastaların %60,9'u birden fazla antihipertansif ilaç kullanıyordu.

• **Sonuç:** Sonuçlarımız uluslararası kılavuzların doktorlarımızın antihipertansif ilaç yazma alışkanlıkları üzerine etkilerinin sınırlı kaldığını göstermektedir. Hastalarımızın takibinde tedavi kılavuzlarına uyumlu antihipertansif ilaç yazma konusunda daha dikkatli olmamız gerektiğini düşünüyoruz.

• **Anahtar Kelimeler:** Hipertansiyon, antihipertansif ilaçlar, hipertansiyon tedavi kılavuzları. **Nobel Med 2010; 6(1): 20-25**

INTRODUCTION

Hypertension, a major but modifiable contributory factor in cardiovascular disease, affects more than 29% of adult population in Turkey.¹⁻³ Cardiovascular events are the major determinants of morbidity and mortality in general population. The primary goal in the treatment of hypertension is to reduce the incidence of adverse cardiovascular events.⁴ Controlling hypertension is a complex problem involving the detection of elevated blood pressure, medical evaluation and treatment, and adherence to treatment. In long-term placebo-controlled trials, the use of antihypertensive drug therapy has been shown to reduce overall mortality, myocardial infarction, and stroke by 8, 15, and 25%, respectively.⁵ The benefits of antihypertensive therapy cannot be achieved unless patients consistently use it. Poor adherence to antihypertensive medications is a key factor contributing to the low rates of blood pressure control in hypertensive patients.⁶ Antihypertensive drug discontinuation rates, however, are much higher in actual practice settings than in long-term clinical trials where adherence is enhanced to provide the best estimate of treatment effect. In long-term trials, antihypertensive drug discontinuation rates range from 5 to 10% per year, with discontinuation rates of up to 50-60% after 6 months having been reported in actual practice.^{5, 7-9} Patients with high blood pressure may fail to take their medication due to chronic nature of

hypertension and its absence of symptoms; other reasons that have been studied include the adverse effects of medications, complicated drug regimens, lack of understanding about hypertension management, lack of motivation and challenge to individuals' health beliefs.¹⁰ Clinical practice guidelines are developed to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. Although the awareness of high blood pressure has improved in the last decades, the percentage of patients whose blood pressure is controlled has remained unchanged and physicians' nonadherence to guidelines might be a factor. In this study, we aimed to evaluate the adherence of clinicians to clinical practice guidelines--specifically those of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (the JNC 7 Report) for the treatment of patients with hypertension.

MATERIAL and METHOD

Study population

This cross-sectional study was carried out in Ankara, Turkey, in 2007. All patients with at least one health care claim indicating hypertension as a diagnosis were selected for initial study entry. All patients who gave consent to be included in the study were recruited by→

Table 1: Descriptive characteristics of the participants by gender			
Characteristics	Female (n= 441)	Male (n= 270)	Total (n= 711)
Age (years)	67.2 ± 10.9	66.2 ± 9.4	66.8 ± 10.4
BMI (kg/m ²)	29.3 ± 6.2	28.1 ± 8.2	28.7 ± 7.2
Hypertension duration (years)	11.9 ± 8.6	11.2 ± 7.6	11.6 ± 8.3
Device*			
Present (n)	350 (79.5%)	224 (83%)	574 (80.8%)
Absent (n)	91 (20.5%)	46 (17%)	136 (19.2%)
Tobacco consumption			
Smoker (n)	85 (19.3%)	74 (27.4%)	159 (22.4%)
Nonsmoker (n)	356 (80.7%)	196 (72.2%)	552 (77.6%)
Education (n)			
Primary school or less	144 (32.7%)	58 (21.5%)	192 (28.4%)
Junior or high school	199 (45.1%)	94 (34.8%)	293 (36.3%)
College or higher	98 (22.2)	118 (43.7%)	216 (30.4%)
Marital status (n)			
Married	247 (56.3%)	225 (83.3%)	472 (66.6%)
Single	20 (4.5%)	9 (3.3%)	29 (4.1%)
Widow	158 (36%)	32 (11.9%)	190 (26.7%)
Divorced	16 (3.2%)	4 (1.5%)	20 (2.6)
Child (n)			
Present	398 (90.2%)	238 (88.1%)	636 (89.5%)
Absent	43 (9.8%)	32 (11.9%)	75 (10.5%)
BMI: Body Mass Index, *Device = Blood pressure measuring device at home			

random selection between January and December 2007. A face-to-face home interview was performed by a group of trained interviewers and participants who were followed up by cardiology, nephrology, internal medicine or family medicine outpatient clinics included in the study. Patients were eligible if they had diagnosis of hypertension according to the JNC 7 report⁴ and at least taking one antihypertensive drug. Patients were excluded if they were not receiving antihypertensive therapy or were prescribed antihypertensive medication for less than two months during the 12-month monitoring period. The study was approved by local ethics committee.

Data collection

Clinical and demographic characteristics for all participants including age, sex, weight, height, marital status, educational level and smoking status were collected. A self-reported medical history was also obtained relating to past history of hypertension, diabetes, hyperlipidemia, coronary artery disease, coronary artery by-pass graft operation and cerebrovascular accident. The level of education was based on the last school from which the patient graduated. Smoking status was classified 'current smoker' or 'non-smoker'. Medications used regularly for the control of hypertension during two

months before interview and classes of prescribed antihypertensive drugs were recorded. The following drug classes were included: ARB and ARB combined with a diuretic (ARB plus), ACEI and ACEI combined with a diuretic (ACEI plus), beta-blockers and beta blockers combined with a diuretic, (CCB), and other antihypertensive drugs were classified as one class. Patients, who use more than one antihypertensive drug, were questioned for antihypertensive drug prescription sequence. All participants asked whether their blood pressure is controlled or not. Participants without a past or present history of high blood pressure, although using drugs which can be used for the management of cardiovascular disease (CVD) independently of their blood pressure-lowering effect, were not obtained as hypertensive. We also excluded those who received other less commonly used classes of antihypertensive drugs. Prescription records for hypertension medications were also obtained from IMS-Health Turkey for the year 2000-2005. Causes of change to other antihypertensive drug were also questioned and recorded.

Data analysis

All statistical analysis were performed using the (Statistical Package For Social Sciences) SPSS program, version 11.5 (SPSS Inc., Chicago, IL, USA) for Windows XP. Demographic and clinical characteristics, including medications were described using frequencies and descriptive statistics. Unless otherwise stated, values are expressed as Mean ± SD. With respect to cardiovascular risk factor differences between men and women, the analyses were performed totally and separately for men and women.

RESULTS

General characteristics

In the initial sample, there were a total of 750 representative patients identified with essential hypertension and using antihypertensive drug. After applying exclusion/inclusion criteria, the final study sample included 711 patients (95%). Of these, 270 (38%) were male. The mean age of the participants was 67.2±10.9 years in females and 66.2±9.4 years in males. The mean BMI was 29.3±6.2 kg/m² in females, and 28.1±8.2 kg/m² in males. The mean duration of hypertension was 11.9±8.6 years in females and 11.2±7.6 years in males. Eighty five (19.3%) of women were currently smoker and 74 (27.5%) of men were smoker. Among women, 22.2% were university graduates and 31.7% were college graduates, and among men, 43.7% were university graduates and 23.3% were college graduates, and others were primary school graduates or less educated. A total of 574 patients (80.8%) had blood →

pressure measurement device at home. The demographic characteristics of study subjects are presented in Table 1. Of all patients 29.2% were diagnosed with diabetes and 63.3% were diagnosed with hyperlipidemia concomitantly. Comorbidities of the patients are shown in Table 2.

Distribution of drug usages

As a first line antihypertensive therapy, ARB + ARB plus are ranked first among all antihypertensive (33.5%), ACEI and ACEI plus ranked second (21.2%), and followed by beta-blockers (14.1%), and calcium channel blockers (12.8%). As a second line antihypertensive therapy, diuretics ranked first (52.8%), beta blockers ranked second (20.6%), CCB ranked third (18.8%), and other classes have being chosen less than 5%. As a third line antihypertensive therapy, diuretics were the first and beta-blockers were the second. The distribution of total antihypertensive drugs was shown in Table 3. Nevertheless, according to the IMS-Health data, ACEI and ACEI plus were the most common sold, beta blockers were the second, CCB were the third and ARBs including diuretic form were the forth common sold antihypertensive drug in Turkey in 2005 (Figure 1). There were 207 diabetic patients with hypertension in the study population and 126 of them (60.9%) were using more than one antihypertensive therapy. Of these patients, 114 (55%) were using ACEI or ARB and 29 (14%) were using beta blockers as a first line antihypertensive therapy. Additionally, 52 diabetic patients (25.1%) were using diuretic and 26 patients (12.5%) were using ACEI or ARB as a second line antihypertensive therapy. Moreover, there were 130 hypertensive patients with coronary artery disease and of these patients, 63 (48.4%) were using ACEI or ARB, 19 (14.6%) were using CCB, 17 (13.1%) were using beta blockers and 10 (7.7%) were using diuretics as a first line antihypertensive therapy. There were 59 patients with a past history of Cerebro-Vascular Accident CVA, and 31 of them (52.5%) were using ACEI or ARB, 11 (18.6%) were using CCB as a first line therapy. There were 447 patients with hyperlipidemia and 245 of them (54.8%) were using ACEI or ARB, 64 (14.3%) were using beta blocker, 50 (11.2%) were using CCB as a first line therapy, and only 146 of them (32.7%) were using statin therapy. The comparison between the distribution of antihypertensive therapy for such associated conditions and JNC VII Recommendations for this compelling indication was shown on Table 4. Among the 711 patients, 278 (39.1 %) were taking one antihypertensive drug, 265 (37.3%) were taking two drugs, 130 (18.3%) were taking three drugs, and 38 (5.4%) were taking four or more drugs. Totally, 60.9% patients found to be using more than one

Table 2: Distributions of patients' comorbidities

Comorbidities	Female	Male	Total
CVA (n)	29 (6.6%)	30 (11.1%)	59 (8.3%)
Diabetes (n)	124 (28.1%)	83 (30.9%)	207 (29.2%)
Hyperlipidemia (n)	284 (64.8%)	163 (60.8%)	447 (63.3%)
Coronary artery disease (n)	50 (11.3%)	80 (29.6%)	130 (18.3%)
CABG	15	26	41
PTCA	11	24	35
Medical therapy	24	30	54

CVA; Cerebrovascular accident, CABG; Coronary artery by-pass graft, PTCA; Percutaneous trans coronary angioplasty

Table 3: The distribution of antihypertensive therapy

Antihypertensive therapy	Female (n=441)	Male (n=270)	Total (n=711)
ARB + ARB plus	199	84	283
ACEI + ACE plus	115	75	190
CCB	123	76	199
BB + BB plus	147	70	217
Diuretic	222	108	330

ARB; Angiotensin II antagonist, ARB plus; ARB combined with a diuretic, ACEI; Angiotensin converting enzyme inhibitor, ACEI plus; ACE-inhibitors combined with a diuretic, BB; Beta blockers, BB plus; Beta blockers combined with a diuretic, CCB; Calcium channel blockers.

antihypertensive drug for hypertension control. 20% of the participants' blood pressures were under control.

Causes of switching to other drug were ineffectiveness of drug 57%, side effects 24.7% and had other causes 18.3%. Among 130 patients 18.2% who switched the drug because of side effects; 43.1% had dry cough, 41.5% had pedal edema, and 15.4% had gastro intestinal side effects.

DISCUSSION

Our major findings are that (i) ARB and ACEI including diuretic forms were the most frequent used antihypertensive drug, (ii) 55% of diabetic patients were using ARB or ACEI as a first line therapy, (iii) 48.4% of hypertensive patients with coronary artery disease were using ACEI or ARB, and 13.1% were using beta blockers as a first line therapy, (iv) 60.9% of the patients using more than one antihypertensive drug for hypertension control.

Hypertension has become a major public problem and awareness and treatment of hypertension have increased substantially in the last decades. Hypertension therapy has reduced the incidence and severity of cardiovascular disease; however, its real benefits are far below its known benefits. Failure to achieve adequate blood →

pressure control is an important problem worldwide. Noncompliance has been implicated as the predominant reason of antihypertensive therapy failure to control blood pressure.^{11, 12} Lifestyle changes, particularly weight loss and reduced dietary sodium intake, contribute to blood pressure reduction; however, most people fail to consistently follow such recommendations. Therefore, antihypertensive agents are required to adequately reduce blood pressure in most patients. There is much variation in prescribing patterns of antihypertensive drugs among countries. In keeping with current guidelines, we considered thiazides diuretics to be appropriate first-line hypertension therapy for patients without specific indications for another drug. The JNC 7 report includes specific indications for certain classes of antihypertensive drugs.⁴ A diuretic, indapamid is currently available in Turkey; however, apart from combination, sole thiazides diuretics are not currently available in Turkey's market.

According to the IMS-Health data, ACEIs and beta blockers are generally the most widely used drugs for the treatment of hypertension in Turkey. Apart from that ACEI, ARB and beta blocker prescribing are increasing in last five years in Turkey (Figure D). However, our results shows that ARB are prescribed as first line antihypertensive drug, ACEI ranked second, beta blockers ranked third and calcium channel blockers ranked fourth. Our finding was supported by the results of Hypertension Incidence in Turkey (HinT) Study, which was published in 2007 on the website of Turkish Society of Hypertension and Renal Diseases.¹³ The difference between the results of these both studies and IMS-Health data might be due to change in the prescribing pattern in last two years generally and regional drug prescription diversity in Turkey. However, it is possible that physicians working in Ankara interact more frequently with drug company representatives, and this may explain some of the variation in prescribing behavior and nonadherence to guidelines. Notwithstanding, as a result, our study shows that physicians did not follow the JNC 7 guidelines in assessing their initial treatment recommendations for patients with comorbidities in Ankara, Turkey.

Nonadherence to guidelines has previously been documented in the literature.¹⁴ Physician adherence to guidelines may be hindered by a variety of barriers. Lack of awareness and familiarity affect physician knowledge of a guideline, and lack of agreement, self-efficacy, outcome expectancy, and the inertia of previous practice are also potential barriers.¹⁵ The role of providers in affecting physician adherence to antihypertensive drug prescription may be important. The main explanatory variable for prescribing antihypertensive drug choices and particularly the driving

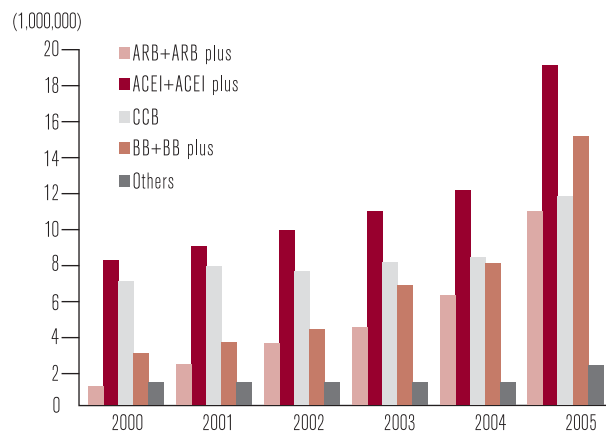


Figure: IMS- Health Turkey data by years

Table 4: The distribution of antihypertensive therapy for associated conditions and JNC VII Recommendations for this compelling indications (+)

	Diuretics	Beta blocker	ACEI or ARB	CCB
Diabetes	25.1 (+)	14 (+)	55 (+)	
CAD	7.7 (+)	13.1 (+)	48.4 (+)	14.6
CVA			52.5 (+)	18.6
Hypertlipidemia		14.3	54.8	11.2

force behind the prescribing of newer drugs, such as ARBs and ACEI seems to be the pharmaceutical marketing pressures.¹⁶ The relationship between specialists and industry might be another factor. Conflicts of interest of opinion leaders may also be an issue. Ankara has a rather high number of opinion leaders in the cardiovascular area that have been active in collaboration with pharmacy industry. Their prescribing behaviors may be followed by general practitioners. The use of drug-samples and educational activities such drug specific meetings or free congress participations at various cities in the world play an active role in trying to influence prescribing behavior among Turkish primary care physicians.¹⁷ For trial-participation to be an effective marketing strategy it is necessary to recruit as many physicians as possible. In many countries doctors are typically paid a bulk sum in the order of \$800 - \$2400 for every patient they enroll in clinical trials.

Antihypertensive drugs have different adverse effect profiles and antihypertensive drug tolerability is an important cause of discontinuation and non-compliance with antihypertensive medications.^{18, 19} Patients may effect physician adherence to guideline by showing resistance or due to drug adverse effect. In the present study, the most common side effects found to be dry cough and pedal edema, and ineffectiveness of drugs found to be 57% to switch to another antihypertensive drug. In addition, to our opinion before switching the drug due to ineffectiveness, adherence of the patient →

should be searched. Our results also show that to achieve adequate blood pressure control more than half of the patients need to use multiple drug classes. While 39.1% of patients using monotherapy, 60.9% of patients found to be using more than one anti-hypertensive drug. Multiple drug therapy might be another factor for physicians' nonadherence to guidelines, especially in hypertensive patients with other comorbidities.

In the past few years, automatic electronic devices have become increasingly popular. As the number and type of blood pressure measurement devices and commercial advertising increased, more people are measuring blood pressure more frequently. In the current study, 80.8% of the patients had an automatic electronic blood pressure devices at home. Self monitoring has some advantages including it is relatively cheap and provides a convenient way for monitoring blood pressure. Additionally, it improves both therapeutic compliance

and blood pressure control.²⁰ Therefore, self monitoring should be more stressed, and devices that have memory or printouts of the readings should be recommended in clinical applications.

There are some limitations to our study. Firstly, the sample size used in our study was small and the study was carried out only in Ankara region. Secondly, our study assessed self reported data that may not reflect accurately actual prescribing practices which may be the reason of the disparity between IMS-Health data and our results.

In conclusion, our results showed that despite wide declaration, guidelines have had limited effect on changing physician behavior. We need to be more careful in achieving antihypertensive therapy in accordance with hypertension guideline. Further large scale studies are needed to improve physicians' awareness to hypertension guidelines.



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