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## EVALUATION OF PATIENTS WITH HYPERTENSION IN THE LIGHT OF THE JNC 7 REPORT: USE OF COMBINATION AND INDIVIDUALISED THERAPY IN UNSATISFACTORY

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Hypertension is a disease that affects a wide range of the population, the control rate was <50% even among those patients known to have hypertension and considered to be receiving active treatment. The aim of this study was to evaluate the patients with hypertension according to the JNC 7 Report, and to assess their use of combination therapy and the adherence to individualized therapy. Patients were recruited from three different centers of Turkey. A questionnaire that comprise 30 questions was administered to each patient. A total of 153 patients (51 men, 102 women) of hypertension were included in the study, 88 (57.5%) of which were under the treatment of combined drug

therapy. The blood pressure control rate of the study group was 58.2% according to blood pressure < 140/90. There was no difference in the control rates among the patients using single-drug and combined drug therapy (p>0.05). The patients who had regular BP measurements had better control rate (p<0.05). The results of this study showed that there are still measures to take for achieving better individualized therapy, and physicians' judgement on the patients' therapy should be made considering the patient-centered care to achieve better results with individualized therapy.

**Keywords:** hypertension; combined drug therapy; individualized therapy

## Introduction

Hypertension is a disease that affects a wide range of the population, especially the elderly after the age of 55. Individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing hypertension. It affects approximately a billion individuals worldwide (1). Although there are many drugs of choice for the treatment of hypertension, the control rate is <50% even among those patients known to have hypertension and considered to be receiving active treatment (2).

'The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure' (JNC 7 Report) provides a new guideline for hypertension prevention and management. There are seven key messages in this report:

In persons older than 50 years, systolic BP of more than 140 mm Hg is a much more cardiovascular disease (CVD) risk factor than diastolic BP

The risk of CVD begins at 115/75 mm Hg, doubles with each increment of 20/10 mm Hg Individuals with a systolic BP of 120 to 139 mm Hg or a diastolic BP of 80 to 89 mm Hg should be considered as pre-hypertensive and require health promoting lifestyle modifications to prevent CVD

Thiazide-type diuretics should be used in drug treatment for most patients with uncomplicated hypertension, either alone or combined with drugs from other classes Most patients with hypertension will require 2 or more antihypertensive medications to achieve goal BP, if BP is more than 20/10 mm Hg above goal BP

Consideration should be given initiating therapy with 2 agents, 1 of which usually should be a thiazide-type diuretic.

The most effective therapy prescribed by the most careful clinician will control hypertension only if patients are motivated (1). There are still obstacles in keeping the BP at the demanded levels. Physicians should pay more attention for the individualized therapy.

This study aimed to evaluate the patients with hypertension according to the JNC 7 Report, and to assess their use of combination therapy and the adherence to individualized therapy.

### Materials and Methods

#### Study population

This research was carried out in May-June 2003 in three different centers of Turkey with different socioeconomic and cultural status. The research group was chosen from the patients of hypertension who have admitted to the three centers during two months. The inclusion criteria was the presence of hypertension.

## Questionnaire

A questionnaire comprising of 30 questions was administered to all of the patients. The questionnaire was performed by face-to-face interview. The first five questions were about the demographic data of the patients. The remaining questions were regarding the diagnosis, and the evaluation at the time of the diagnosis, adherence to diet and the prescribed drug therapy, the duration of control by the physician, the change in the firstly prescribed drugs, the measures taken when the blood pressure (BP) is high, the use of combination therapy, and the existence of comorbid diseases.

## Statistical analysis

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Statistical analysis was performed by using SPSS statistical package (Version 11.0, SPSS Inc., Chicago, IL, USA) for Windows. Chi-square tests were used to determine the differences between the groups. The level of statistical significance was set at p < 0.05.

## Results

A total of 153 patients of hypertension were included in the study. There were 51 men (33.3%) and 102 women (66.6%) with a mean age of 57.2  $\pm$  11.9 (range, 25-88). BP control was better when age was <55 (Table 1).

Table 1 BP Control According to Gender, Age, and Education					
	n	BP>140/90		<b>X</b> /2	(p-value)
		Number	%		
Total	153	64	41.8		
Gender					
Male	51	21	41.1		
Female	102	43	42.1	0.01	>0.05
Age					
<55	71	23	32.3		
³55	82	42	51.2	4.78	<0.05
Education					
Primary school and less	87	42	48.2		

High school and lycee	33	11	33.3		
University	33	11	33.3	3.44	<0.05

The most common educational status was primary school graduates (34.2%), followed by graduates of University (%21.5). The mean BP measurements at the time of the diagnosis were 5. Laboratory examinations were performed for 94 (62.7%) patients after diagnosis. Eighty-six (56.2%) patients stated that they could get enough information about the treatment of the disease. Sixty- seven (44.4%) patients were on diet after diagnosis. The mean of the duration of diet was  $36.5 \pm 91.8$  months. One hundred and nineteen (77.7%) patients were currently on diet.

One hundred and forty-six (95.4%) patients were regularly taking their drugs. One hundred and fifteen (75.1%) patients were having regular BP measurements. There was a statistically significant difference in the BP control of among the patients having regular and irregular BP measurements, where the patients having regular BP measurements had better control (p<0.05) (Table 2). The frequency of blood pressure measurements was once in 9.0  $\pm$  24.7 days. The mean and SD of the Body Mass Index (BMI) was 30.2  $\pm$  5.4.

# Table 2 BP Control According to Enough Knowledge, Diet,Regular Intake of Drugs, Regular Measurement of BP, VisitingDoctor when BP is High, and Body Mass Index (BMI).

	BP>140/90		<b>X</b> /2	(p-value)
	Number	%		
Enough knowledge				
Yes	36	41.8		
No	21	62.4	1.36	>0.05
On diet				
Yes	46	38.6		
No	12	35.2	0.02	>0.05
Drug use				
Regular	60	41.0		
Irregular	1	14.3	1.04	>0.05
BP measurement				
Regular	39	34.0		
Irregular	23	60.5	7.33	<0.05
Doctor visit				
Yes	7	26.0		
No	52	41.3	1.61	>0.05
BMI				

Normal	13	50.0		
Overweight and Obese	47	37.1	1.03	>0.05

The mean duration of doctor visit was once in  $5.24\pm5.19$  months. The percentage of patients with systolic BP over than 140/90 mm Hg was 41.8. There were 24 (15.6%) patients visiting their doctors when their BPs were high, 30 (19.6%) taking one more of their antihypertensive drug, 54 (35.2%) eating garlic, and 65 (42.4%) eating lemon.

There were 76 (49.6%) patients still using the initial drugs. The patients who have changed using their initial drugs have used them for  $30.6 \pm 31.5$  months. The main reason for changing the drug was the insufficiency of maintaining the desired control level (45.6%). There were 88 (57.5%) patients using combined drug therapy, and 32 (20.9%) patients have started using combination therapy at diagnosis. The most commonly used combination was angiotensin converting enzyme (ACE) inhibitors and diuretics, with 38 (24.8%) patients. There was no difference between the BP controls of the patients using monotherapy or combination therapy (Table 3).

Table 3 Drug Groups and BP Control				
	BP>140/90		<b>X</b> /2	(p-value)
	Number	%		
Monotherapy*	23	35.3		
Combination therapy	35	39.7	0.15	>0.05

\*Monotherapy drugs: ACE inhibitors, ARBs, BBs, CCBs, Diuretics, and a-1 Blockers

There were 63 (41.1%) patients who had stage 2 hypertension at diagnosis, and 29 (46%) of these were started on combination antihypertensive therapy. Of the 42 patients using single-drug therapy and with initial diagnosis of stage 2 hypertension, 26 (61.9%) had BPs at goal. The mean duration before starting the second drug was  $22.9 \pm 33.1$  months. The BP control rate of the study group according to <140/90 was 58.2%.

The most common comorbid disease was angina pectoris, and the use of drugs was generally compliant with the recommended drugs for compelling conditions. Of the 21 diabetes mellitus patients, 12 (57.1%) were using ACE inhibitors, 9 (42.8%) were using calcium channel blockers (CCBs), 4 (19%) were using angiotensin receptor blockers (ARBs), and 1 (4.7%) was using  $\beta$ -blockers (BBs). There were 11 (39.2%) patients using BBs, and 11 (39.2%) patients using long-acting CCBs among the patients who had angina pectoris. Of the 7 patients who had myocardial infarction, 5 (71.4%) were using BBs, and 5 (71.4%) were using ACE inhibitors.

#### Discussion

The results of this study that the BP control rate of 58.2% shows us the necessity of taking measures for increasing this rate.

The present study has some limitations; we have not questioned the exercise conditions of the patients, and the dietary intake of salt and saturated fats. Alcohol consumption is not questioned as well. However, the data obtained from the percentage of high body mass index (BMI) strongly suggests that there are yet a lot measures to take in order to achieve optimal lifestyles, though the patients think that they are on diet. The small number of patients in disease subgroups was another limitation.

It has been stated in some studies that BP control can be achieved in most patients with hypertension, but the majority will require 2 or more antihypertensive drugs (3,4). The presence of the use of combined drug treatment by 88 of the patients in this study shows that this is true for our patients as well. However, the low percentage of BP control in this group (60.2%) tells us that they still need either an increase of dosage or addition of another drug in the treatment regimen.

The reasons for inadequate BP control are stated as failure of prescribing lifestyle modifications, adequate antihypertensive drug doses, or appropriate drug combinations (1). In this study, 79.2% of the patients stated that they were still on diet, 50.4% of the patients changed the initial antihypertensive drugs, 20.9% of the patients started the treatment as combination treatment, reaching 57.5%. In spite of these, there was still lack of achievement of desired BP control levels in more than half of the patients. This may indicate that it is still necessary to evaluate the use of appropriate drug or drug combinations. Although the patients stated that they were on diet, the calorie intakes should be calculated to figure out whether they were performing a sufficient diet or not. Treating systolic BP and diastolic BP to targets that are less than 140/90 mm Hg is associated with a decrease in CVD complications (1). In patients with hypertension with diabetes and renal disease, the target BP is less than 130/80 mm Hg (5,6). The control rate of 58.2% in this study was low and the control rate was even lower (19%) for the patients with diabetes mellitus.

Major lifestyle modifications with BP lowering effects cause weight reduction in those individuals who are overweight or obese (7,8). There were 127 patients with overweight or obese status in the study group, indicating the necessity of dealing with this inconvenient condition individually for each patient. Patients must be motivated to loose weight and to perform exercise regularly. Physicians must be able to motivate patients for achieving lifestyle modifications. It is a high possibility to start drugs to the patients without giving any chance for lifestyle modifications.

Excellent clinical trial outcome data prove that lowering of BP with several classes of drugs such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), calcium channel blockers (CCBs), and thiazide-type diuretics will all reduce the complications of hypertension (9-11). Thiazide type-diuretics have been the basis of antihypertensive therapy in most outcome trials (11). When BP is more than 20/10 mm Hg above the target, consideration should be given to initiating therapy with 2 drugs, either as separate prescriptions or fixed-dose combinations (1). The use of antihypertensive drugs in our study is suitable for both patients with and without compelling indications. The lack of a higher control rate has a wide range of possible

reasons, which cannot be attributed only to the use of appropriate or inappropriate use of both monotherapy and combination therapy.

Once antihypertensive drug therapy is initiated, most patients will return for follow-up and adjustment of medications at approximately monthly intervals until the BP target is reached. After BP is at target and stable, follow-up visits can usually be at 3- to 6-month intervals (1). The patients in the study group visited their doctors in intervals less than 6 months, but the effectiveness of these doctor visits were questionable considering the high rate of uncontrolled patients. Only 24 (15.6%) patients declared that they visited their doctors when their BPs were high. Most of the patients with chronic diseases probably visited doctors for prescription of drugs without being evaluated for the current control status of the disease, which must be differentiated from the visits made with the demand of disease evaluation.

In patients with hypertension and stable angina pectoris, the first drug of choice is usually a  $\beta$ -blocker. Alternatively, long acting CCBs can be used (1). The use of these drugs was 39.2% in the study group, which could be increased. In patients with acute coronary syndromes (unstable angina or myocardial infarction), hypertension should be treated initially with  $\beta$ -blockers and ACE inhibitors, with addition of other drugs as indicated for the control of BP (12). In patients with postmyocardial infarction, ACE inhibitors,  $\beta$ -blockers, and aldosterone antagonists have proven to be most beneficial (13-16). The use of ACE inhibitors and  $\beta$ -blockers in patients who had myocardial infarction in the study group was 71.4%, which could be evaluated as a satisfactory use of the recommended drugs.

Thiazide diuretics,  $\beta$ -blockers, ACE inhibitors, ARBs, and CCBs are beneficial in reducing CVD and stroke incidence in patients with diabetes (17-19). The ACE inhibitors and ARBs have demonstrated favourable effects on the progression of diabetic and nondiabetic renal disease (20-25). The diabetes mellitus patients in the study group were using drug groups, which are recommended in the JNC 7 Report. The low control rates of BP for the patients with diabetes mellitus suggests that this is independent of the type of the used drug or combination therapy, and is likely due to the lack of increasing the dosage of the drug or drugs, or addition of another drug to either monotherapy or combination therapy.

In conclusion, the control rate is at desired level when Healthy People 2010 goal of 50% control is considered, but the control rates for the compelling condition diabetes mellitus is still far from the target level (1). The aim of controlling the hypertension of 50% of the patients is not satisfactory when the patients are considered individually, because the remaining 50% will still be susceptible to all of the complications of the disease. There are still many measures to take from the point of individualized therapy The physicians' judgement on the patients' therapy should be made considering the patient-centered care in order to achieve better results with individualized therapy. In addition, more attention should be paid on the patients by spending appropriate time to eliminate the barrier factors in achieving the goal BP.

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