

# The drug adherence and lifestyle factors that contribute to blood pressure control among hypertensive patients

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## ABSTRACT

**Objectives:** To investigate drug adherence and lifestyle behaviors affecting the blood pressure (BP) control among hypertensive patients that have uncontrolled and controlled BP.

**Methods:** Seventy-eight uncontrolled BP and 98 controlled BP hypertensive patients matched on age, gender, time since hypertension diagnosis and the number of antihypertensive drugs used were investigated using a standardized questionnaire to evaluate lifestyle behaviors, drug adherence, the use of complementary and alternative medicine, and health related quality of life. Drug-drug interactions were evaluated with an electronic drug reference software.

**Results:** Not taking therapy when feeling better was observed significantly more frequently in the uncontrolled hypertensive group (OR: 0.297, %95 CI: 0.115-0.770). Uncontrolled BP hypertensive patients live more frequently in extended family settings ( $p = 0.043$ ), they sleep less controlled BP hypertensive patients (OR: 0.749, %95 CI: 0.605-0.929). The groups did not differ statistically in terms of Complementary and Alternative Medicine (CAM) use ( $p = 0.795$ ) and informing doctors about the use of CAMs ( $p = 0.910$ ). The EuroQol five-dimensional 3 level (EQ5D3L) questionnaire Visual Analogue Scale (VAS) score was significantly higher in the control group ( $p = 0.011$ ). In both groups over 70% of patients should be monitored for therapy due to drug interactions evaluation.

**Conclusions:** Our study shows that increasing the drug adherence and sleeping hours and living in the nuclear family is associated with improvement in blood pressure control and health related quality of life. A comprehensive approach and good patient-physician communication and trust are essential for well-managed hypertension.

**Keywords:** Hypertension, drug adherence, drug interaction

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Hypertension is responsible for about 4.5% of the recent overall disease load in the world, and leads to cerebrovascular diseases, ischemic heart diseases, and cardiac failure. Treatment can significantly reduce these devastating problems [1]. Success rates in treatment and risk management vary among countries. Using a blood pressure (BP) hypertension cut-off point of 140/90 mmHg, 29% of patients in the



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United States of America had their BP controlled. The same ratio for European countries ranged from 5-10%, 17% for Canada, and the highest rate was 38% in Barbados [2, 3]. Also, in Turkey, the BP control rates among hypertensive patients are low and vary between 16%-30% according to geographical regions [4, 5].

In addition to drug treatment, lifestyle changes including diet and exercise are recommended for patients with hypertension [6].

Adherence to antihypertensive treatment has been shown to be low in literature, with similar findings reported in Turkey [5, 7]. Most patients do not adhere to recommended lifestyle changes regarding diet and exercise [8].

A major proportion of patients who receive drug treatment for hypertension also uses complementary and alternative medicine (CAM) [9]. In Turkey, the research done in Eastern Anatolia region shows that majority of patients reported using CAM [10].

Drug-drug or drug-herb interactions is a necessary risk that should be kept in mind when prescribing antihypertensive agents. A study done by Carter *et al.* [11] reported a very high frequency of potential drug interactions with agents used for hypertension treatment.

It has been shown in literature that patients with hypertension have poorer health related quality of life (HRQoL) than normotensives [12, 13]. Hypertensive patients are a vulnerable group in the health system and merit special attention due to low HRQoL among this group increases the risk of cardiovascular events [14].

To our knowledge, there is limited information regarding Turkish hypertensive patients' lifestyle behavior and antihypertensive treatment adherence affecting BP control. In the present study, we aimed to investigate drug adherence, drug-drug interactions, complementary alternative medicine use, lifestyle behaviors affecting the blood pressure and quality of life among patients has uncontrolled and controlled blood pressure.

## METHODS

This study was undertaken in the Pharmacology Department of Istanbul Faculty of Medicine, Clinical Pharmacology Division, from June to November

2014.

Seventy-eight randomly selected patients with uncontrolled hypertension and 98 controls with controlled hypertension matched on age, sex, the number of hypertensive agents used and time since hypertension diagnosis were enrolled in the study.

Patient inclusion criteria were as follows: aged between 38 and 74 years, hypertension diagnosis history of at least 6 months and use of at least one antihypertensive medication.

After participants were informed about the study and their informed consent obtained, data were collected through researcher-administered patient interviews using a standardized questionnaire consisting of sociodemographic variables such as age, sex, marital status, and educational level. It also comprised clinical variables such as other chronic diseases seen during the diagnosis of hypertension, other drugs used, and drug adherence-related questions, the use of CAM, lifestyle behaviors, and quality of life. To determine the participants' quality of life, we used EuroQol five-dimensional 3 level (EQ5D3L) questionnaire [15]. Indexing was undertaken as with the method used in the Turkish validation and reliability study of Eser *et al.* [16].

Patients' height was measured using a height rod and weight was measured with a digital scale. Blood pressure and heart rate were measured using a calibrated digital blood pressure monitor. Drug interactions were evaluated with an electronic drug reference software, Lexi-Comp's Comprehensive Drug-to-Drug, Drug-to-Herb, and Herb-to-Herb Interaction Analysis Program (Lexi-Interact Online).

Controlled hypertension was defined as systolic blood pressure (SBP)  $\leq$  139 mmHg and/or diastolic blood pressure (DBP)  $\leq$  89 mmHg for non-diabetic patients, and as SBP  $\leq$  139 mmHg and/or DBP  $\leq$  84 mmHg for diabetic patients, based on the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC) guidelines [6]. Individuals who had blood pressure levels above these values were defined as uncontrolled hypertensive patients. The study was approved by the Ethics Committee of Istanbul School of Medicine on 10/06/2014.

## Statistical Analysis

The descriptive statistics used in the study were

mean ± standard deviation (SD) for normally distributed variables, median and IQR for non-normally distributed variables, as well as frequency counts and percentages of participant characteristics. Independent samples t-test or Mann-Whitney U were used to compare groups' variables. The Chi-square and the Likelihood ratio were used to evaluate categorical variables. OR and 95% CI is calculated using Logistic regression. The Statistical Package for Social Sciences (SPSS) version 21 was used to analyze data, and *p* < 0.05 was considered to be significant.

## RESULTS

The age, sex distribution, body mass index (BMI), education status, the number of antihypertensive medications used, the time since hypertension diagnosis, SBP and DBP and heart rate are summarized in Table 1.

Not taking therapy when feeling better was observed significantly more frequently in the uncontrolled hypertensive group (OR: 0.297, %95 CI: 0.115-0.770) (Table 4). Cases; uncontrolled hypertension patients tend to live in extended family settings (*p* = 0.043) (Table 1) and sleep less than controls OR: 0.749 (%95 CI: 0.605-0.929) (Table 4). The groups did not differ statistically in terms of Complementary and Alternative Medicine (CAM) use (*p* = 0.795) and informing doctors about the use of CAMs (*p* = 0.910) (Table 2). In both groups over 70% of patients should be monitored for therapy due to drug interactions evaluation (Table 2). Less than half of both groups partook in regular physical activity but there was no statistically significant difference between the two groups (Table 3). There were no significant differences in smoking and alcohol drinking habits between the groups (Table 3). No significant differences were found in eating frequency habits between the groups (Table 3). The EQ5D3L

**Table 1.** Characteristics and health parameters of study population

	<b>Uncontrolled hypertension n = 78)</b>	<b>Controlled hypertension n = 98)</b>	<b>p value</b>
<b>Age (years)</b>	58.39 ± 8.84	57.85 ± 7.63	0.664 <sup>§</sup>
<b>Sex</b>			
<b>Male</b>	21 (26.9%)	23 (23.5%)	0.599*
<b>Female</b>	57 (73.1%)	75(76.5%)	
<b>BMI (kg/m2)</b>	30.75 ± 4.7	31.06 ± 5.51	0.698 <sup>§</sup>
<b>Antihypertensive drugs used daily</b>	2 (1-2)	2 (1-2)	0.783 <sup>¶</sup>
<b>Time from hypertension diagnosis</b>	8 (3-14)	8 (4-11)	0.911 <sup>¶</sup>
<b>Education</b>			
<b>Can't read</b>	2 (2.6%)	0(0%)	
<b>Collage</b>	60 (76.9%)	67 (68.4%)	0.056 <sup>¥</sup>
<b>University and post graduate</b>	16 (20.5%)	31 (31.6%)	
<b>Family</b>			
<b>Nuclear</b>	57 (73.1%)	80 (81.6%)	
<b>Extended</b>	18 (23.1%)	10 (10.2%)	<b>0.043¥</b>
<b>Divorced/Widowed</b>	3 (3.8%)	8 (8.2%)	
<b>SBP</b>	150 (140-160)	120.5 (116-130)	<b>&lt; 0.0001<sup>¶</sup></b>
<b>DBP</b>	80 (73.7-90)	75 (70-80)	<b>&lt; 0.0001<sup>¶</sup></b>
<b>Heart Rate/min</b>	79 (71-86)	76 (72-82)	0.228 <sup>¶</sup>

Data are shown as mean±standard deviation or median (IQR) or number (percent). SBP = systolic blood pressure, DBP = dastolc blood presure, §-Independent Samles t-test, \*-Pearson Chi Square test, -Independent samples Mann Whitney U test, ¥-Likelihood Ratio test.

**Table 2.** Number of drugs used, drug intake habits and drug interaction

	<b>Uncontrolled hypertension n = 78)</b>	<b>Controlled hypertension n = 98)</b>	<b>p value</b>
<b>Forgets to take drugs</b>	27 (34.6%)	38 (38.8%)	0.570*
<b>Doesn't take drugs when feel better</b>	16 (20.5%)	8 (8.2%)	0.018*
<b>Forgets to prescribe drugs when ends</b>	16 (20.5%)	22 (22.7%)	0.730*
<b>Drug interaction ( n = 70 vs 82)</b>			
<b>Drug interaction A</b>	14 (20%)	9 (11%)	0.193 <sup>‡</sup>
<b>Drug interaction B</b>	1 (1.4%)	0 (0%)	
<b>Drug interaction C</b>	51 (72.9%)	62 (75.6%)	
<b>Drug interaction D</b>	3 (4.3%)	9 (11%)	
<b>Drug interaction X</b>	1 (1.4%)	2 (2.4%)	

Data are shown as number (%). Drug interaction Risk Rating = A - No Known Interaction, B - No Action Needed, C - Monitor Therapy, D - Consider Therapy Modification, X - Avoid Combination, \*-Pearson Chi Square test, <sup>‡</sup>-Likelihood Ratio test.

**Table 3.** CAM use, eating habits, regular exercise and EQ5D3L index and VAS score

	<b>Uncontrolled hypertension n = 78)</b>	<b>Controlled hypertension n = 98)</b>	<b>p value</b>
<b>CAM use</b>	20 (25.6%)	28 (28.6%)	0.665*
<b>Tells to doctor that use CAM</b>	10 (43.5%)	13 (53.5%)	0.910*
<b>Smokers</b>	14 (17.9%)	27 (27.6%)	0.134*
<b>Drinks alcohol</b>	14 (17.9%)	17 (17.3%)	0.917*
<b>Mean meals per day</b>	3 (2-3)	3(2-3)	0.219 <sup>¶</sup>
<b>Number of meals except main meals</b>	2 (1-4)	3 (1-4)	0.742 <sup>¶</sup>
<b>Do regular physical activity per week</b>	29 (37.2%)	31 (31.6%)	0.441*
<b>EQ5D3L index</b>	0.725 (0.62-0.845)	0.743 (0.656-1)	0.300 <sup>¶</sup>
<b>EQ5D3L VAS score</b>	75 (50-80)	80 (70-90)	0.011 <sup>¶</sup>

Data are shown as median (IQR) or number (percent). CAM = complementary and alternative medicine, EQ5D3L = EuroQol five-dimensional 3 level, VAS = Visual Analogue Scale, <sup>‡</sup>-walking or exercising at least 5 days per week not less than 30 minutes, \*-Pearson Chi Square test, <sup>¶</sup>-Independent samples Mann Whitney U test

**Table 4.** Independent predictors of blood pressure with logical regression analysis

	<b>Uncontrolled hypertension n = 78)</b>	<b>Controlled hypertension n = 98)</b>	<b>Odds Ratio (%95 CI)</b>	<b>p value</b>
<b>Doesn't take drugs when feel better</b>	16 (20.5%)	8 (8.2%)	0.344 (0.139-0.854)	<b>0.021</b>
<b>Living in extended family</b>	18 (23.1%)	10 (10.2%)	2.526 (1.086-5.878)	<b>0.031</b>
<b>Sleeping (hours per day)</b>	6.53 ± 1.78	7.13 ± 1.45	0.789 (0.647-0.962)	<b>0.019</b>

Data are shown as mean ± standard deviation or number (percent).

Visual Analogue Scale (VAS) score was significantly higher in the control group ( $p = 0.011$ ) (Table 3). Further data are not shown here.

## DISCUSSION

Lower drug adherence when feeling better, living with an extended family, sleeping less and a poorer health related quality of life of cases than controls plus the need for therapy monitoring a majority of patients due to drug interactions can be listed as main findings in our research.

Drug adherence is important in blood pressure management. Some qualitative research on factors of medication adherence in patients with hypertension found that feeling well and absence of hypertension symptoms were disease-specific barriers [17]. A study by Sengul *et al.* [18] reported that Turkish hypertensive patients have improved awareness about being hypertensive between 2003 and 2012. With regards to adherence to therapy, Altun *et al.* [5] reported that most of the Turkish hypertensive patients declare that they follow the recommendations.

Better antihypertensive drug adherence and BMI lower than 30 (kg/m<sup>2</sup>) are found to be predictors of controlled BP in Turkish hypertensive patients [19]. In our study, forgetting to take medication and requirement for prescription renewal did not differ significantly between the groups as reasons for non-adherence, but not taking therapy when feeling better was observed significantly more frequently in the uncontrolled hypertensive group (20.5%) when compared to the controlled hypertensive group (8.2%). In a qualitative study by Wai *et al.* [20] on lowering blood pressure medications, one in twenty patients declared that they did not take their drugs when they felt well [32]. As regards to treatment, compliance was better among those taking one antihypertensive tablet per day, those who had never changed their antihypertensive regimen, and those who had never changed their physician [7]. Altun *et al.* [5] reported that Turkish hypertensive patients that used one medication do not adhere to therapy by 15 %.

Family and friends' social support is important in the management of chronic diseases and differs in various cultures. A study of Karakaş *et al.* [21] showed that social support of family and friends are higher in

hypertensive patients than in asthmatic patients. In our study, we found that hypertension control rates in nuclear family settings were higher compared with extended families. In contrast, a study conducted in Japanese hypertensive patients living in the nuclear family has been found to have higher systolic BP than patients living in extended families [22]. In a study from Turkey evaluating cardiovascular risk factors in postmenopausal women found hypercholesterolemia is a risk factor in nuclear family setting but there was no correlation between hypertension and family structure [23]. When we evaluate our study result as female gender, our results also do not support female gender and nuclear family. Gender may be a factor on nuclear family setting and better blood pressure control. Unlike to our study population, Sekuri *et al.* [23] investigated rural population. Family structure and blood pressure control relation is interesting and warrants further attention.

Carter *et al.* [11] showed that there is a potential high drug interaction associated with increasing age and number of drugs among hypertensive patients.

Sleeping disorders are well known for increasing a wide variety of health conditions. Hypertensive patients' sleep duration is associated with ischemic or nonspecified stroke mortality in the Singapore Chinese study and both short and long sleeping duration increased the risk [24]. To our best knowledge, there are missing data regarding hypertensive patients' habitual sleeping time in Turkey. But a recent article in pediatric population aged 11-17 reported that increased blood pressure is correlated with sleeping less than 8 hours a day [25]. A small sample sized interventional study to increase average nightly sleep duration about 30 minutes resulted in the reduction of beat-to-beat systolic and diastolic BP in hypertensive and pre-hypertensive subjects [26]. Our study also found that habitual higher sleeping duration is related to better blood pressure control but we need further evidence to recommend sleep time adjustment as lifestyle modification in the hypertensive population. Evaluating patient for insomnia and if necessary consulting a sleep center may be beneficial. According to drug-drug interaction evaluation, groups did not differ significantly but need to monitor therapy (72.9% vs 75.6%) is high and considering change in therapy is needed in about 4% in cases and 11% in controls. In the study done in Croatia drug interaction

in elder hypertensive patients was reported to be higher, being over 90% for considering to monitor therapy and about 20% for considering to change the therapy [27].

In the present study, CAM use was high (25.6% vs 28.6%) and about 50% had not informed their physicians about their CAM use. Similar results were found by Tan *et al.* [10] who found more than 2/3 of the patients use CAM and most of them do not talk to their physician about this use.

Hypertensive patients can adopt different lifestyle changes for improving BP control and reducing CVD risk [28]. Increasing physical activity, smoking cessation, salt reduction are important targets that should be considered in blood pressure control.

In our research, less than half of both groups (37.2% vs 31.6%) adhered to the recommendation for physical activity for adults of 5 days a week not less than 30 minutes per day [29].

In literature, it is shown that alcohol consumption raises the prevalence of hypertension compared to lifetime non-users [30]. Increase in alcohol consumption has been found to be associated with increases in BP among hypertensive patients in Turkish men [31]. In our study, we found that alcohol consumption is frequent (one in five hypertensives) in both groups and doesn't differ statistically.

We found that smoking rates among hypertensive patients between cases and controls (17.9% vs 27.6%) is far from cessation recommendations and doesn't differ significantly among uncontrolled and controlled hypertensives. Neuhauser *et al.* [32] also reported similar rates of smoking (15%) among hypertensive patients.

Patients with a chronic condition such as hypertension, diabetes, dyslipidemia or cardiovascular disease tend not to adhere to diet recommendations guidelines [32]. In obese people, it is found that they have 1.4 main meal per day and have about 4.2 eating occasions per day [33]. In our study, both groups' patients have similar eating frequency patterns as they have 3 mean meals per day and in total 5 (4-6) eating occasions per day.

In a study done by Ucan *et al.* [34] HRQoL was found to be lower in Turkish hypertensive patients when compared to diabetic patients and diabetes and hypertensive conditions combined. It has been shown in literature that with the intensification of

antihypertensive treatment, HRQoL is improved [35, 36]. We found that HRQoL is lower in the uncontrolled BP group. In this context the medication therapy should be evaluated for possible drug interactions.

### Limitations

Our study has some limitations. Sample size is one of the limitations and study design leads to a potential bias due to subjective evaluation.

### CONCLUSION

Our study shows that increasing the drug adherence and sleeping hours and living in the nuclear family are associated with improvement in blood pressure control and health-related quality of life. Also, less physical activity, lack of awareness about drug adherence and frequent use of CAM was seen in our study groups. A comprehensive approach and good patient-physician communication and trust are essential for well-managed hypertension. Higher VAS scores health-related quality of life subjective rating represent an improvement in the quality of life and can be a therapeutic motivation and goal for patients with hypertension and could be included in physicians' patient information booklets.

### Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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