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Effects of Selective Serotonin Reuptake Inhibitor Treatment on Blood Pressure in Resistant Hypertensive Patients with Anxiety Disorder

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ABSTRACT

Objectives: This study aimed to evaluate the effects of selective serotonin reuptake inhibitor (SSRI) treatment on blood pressure (BP) control in resistant hypertensive patients with anxiety symptoms.

Methods: This interventional study was conducted between January 2021 and March 2022 at a family medicine outpatient clinic. Patients with primary hypertension (HT), uncontrolled with monotherapy, and scoring ≥16 on the Beck anxiety inventory were included. All were switched to combination antihypertensive therapy. Those who accepted SSRI treatment constituted the case group, while those who declined formed the control group. Demographic and clinical characteristics were recorded. BP was measured at baseline and after 1 month.

Results: Ninety-one patients were included, 30 (33.0%) male, the median age was 53.5 (35.0–68.0) years. Of the participants, 72 (79.1%) received combined therapy plus SSRI, while 19 (20.9%) received combined therapy only. After 1 month, systolic BP decreased by 15.0 (1.0–22.0) mmHg and diastolic BP by 13.0 (4.0–18.0) mmHg in the case group, compared to decreases of 8.0 (1.0–17.0) mmHg and 6.0 (2.0–13.0) mmHg in the control group (respectively, $p<0.001$ and $p<0.001$).

Conclusion: SSRI therapy provided significantly greater reductions in both systolic and diastolic BP compared with combination antihypertensive treatment alone. Anxiety should be considered an important factor in resistant HT, and psychological as well as pharmacological interventions may enhance treatment outcomes.

Keywords: Antihypertensive agents, anxiety disorders, blood pressure, serotonin reuptake inhibitors

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INTRODUCTION

Hypertension (HT) is one of the leading causes of cardiovascular mortality and morbidity and is a global public health problem.[1] The primary aim in the management of HT is to maintain an optimal blood pressure (BP) and prevent these complications, but this cannot be achieved in a group of patients despite appropriate pharmacological treatment.[2] While secondary causes of HT may come to mind in this condition called resistant HT, an important factor that should not be ignored is psychosocial factors, such as anxiety.[3]

Anxiety disorders are frequently observed in the community and may lead to activation of the sympathetic system, which is not desirable in patients with HT, and thus may lead to an increase in BP.[4,5] Sympathetic activation increases cardiac output and also increases peripheral vascular resistance, and shows this effect. Another problem that may complicate BP management in anxious individuals is that these individuals have lower medication compliance

and unhealthy life preferences, including alcohol, smoking, and poor eating habits, more frequently compared to the general population. In addition, the COVID-19 outbreak increased the anxiety levels of patients and also affected their medical treatment preferences, leading them to move away from medical treatments.[6] In the literature, it is observed that the frequency of HT tends to increase with increasing anxiety level.[7] However, most of the studies conducted on this subject are observational studies, which are not suitable for establishing a causal relationship. The aim of this study was to investigate the effects of the selective serotonin reuptake inhibitor (SSRI) on BP in resistant HT patients with anxiety symptoms.

METHOD

This interventional study was conducted between January 2021 and March 2022 at the Family Medicine outpatient clinic of Maçka Ömer Burhanoğlu Physical Therapy and Rehabilitation Hospital. Patients with primary HT who had been regularly using angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, or thiazide diuretics for at least 1 month, but who failed to achieve effective BP control with monotherapy, and who scored 16 or higher on the Beck anxiety inventory (BAI), were included in the study. Patients were excluded if they had secondary HT, irregular use of antihypertensive medication, contraindications to current therapy (such as beta-blocker use in asthma), or had recently experienced a major life event that could affect BP control, including severe trauma, new sources of stress, or the loss of a loved one.

Patients who fulfilled the inclusion criteria and consented to be included in the study were first asked for routine follow-up and routine biochemical tests in terms of causes that may suggest secondary HT. At this stage, no patient suggestive of secondary HT was identified. At least 5-day home BP values requested from the patient at the previous visit were analyzed, and all patients also underwent office BP measurement by the same clinician in accordance with the guidelines. Office BP values were recorded as the patient's first systolic and diastolic BP values in mmHg. Patients with discordance between office and home BP measurements were re-evaluated in terms of white coat HT and major life events.

The decision to switch to combination therapy was shared with the patient and an appropriate combination was initiated in accordance with the guidelines, taking into account the patient's comorbidities. Patients who did not accept the treatment were excluded from the study. In addition, an appropriate SSRI group drug was started in patients who were clinically evaluated and whose BAI scores were moderate/high. The group receiving SSRI treatment was taken as the case group and the patients who did not accept SSRI treatment were taken as the control group. After 1 month of follow-up, office BP values were measured again. Age, gender, height, and weight values of the patients were also recorded.

Data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) 25.0 (SPSS Inc., Chicago, IL, USA) package program. The conformity of the data to normal distribution was evaluated by the Shapiro–Wilk test. Descriptive statistics were given as median (min-max) for quantitative data and frequency and percentage for categorical variables. The significance of the difference between two groups in terms of median values was analyzed by Mann–Whitney U test and the Pearson Chi-Square test for nominal variables. Spearman correlation analysis was used to evaluate the relationship between continuous variables. Statistical significance level was taken as $p<0.05$.

RESULTS

The study included 91 participants, 30 (33.0%) male and 61 (67.0%) female. The median age of the participants was 53.5 (35.0–68.0) years, and the median body mass index was 33.5 (27.4–39.3) kg/m2. While 72 (79.1%) of the participants were in the case group, 19 (20.9%) were in the control group. Demographic and clinical characteristics of the participants according to treatment groups are summarized in Table 1.

While 33 (36.3%) of the participants were smokers, 23 (69.7%) of them were in the case group, and 10 (30.3%) of them were in the control group ($p=0.095$).

At the follow-up visit performed one month later, systolic BP had decreased by 13.0 (2.0–22.0) mmHg and diastolic BP by 11.0 (2.0–18.0) mmHg. These values were 15 (1.0–22.0) mmHg and 13.0 (4.0–18.0) in the case groups, respectively, while they were 8.0 (1.0–17.0) and 6.0 (2.0–13.0) in the control group (respectively, $p<0.001$ and $p<0.001$).

No significant relationship was found age between BP measurements, such as first and last systolic and diastolic BP measurements, and systolic and diastolic BP difference ($p>0.05$). There was a significant relationship found between height and first diastolic BP or diastolic BP difference, while no relationship was found between first and last systolic BP, systolic BP difference, and last diastolic BP (respectively, $r=0.223$ and $p=0.034$; $r=0.240$ and $p=0.022$; $p>0.05$). On the other hand, a significant relationship was found between weight and first and last systolic BP, first

Table 1. Demographic and clinical characteristics of participants according to treatment groups

	Case group (n=72)	Control group (n=19)	p
Age (years)	53.5 (35.0–68.0)	56.0 (48.0–65.0)	0.086
Height (cm)	162.0 (149.0–180.0)	160.0 (155.0–178.0)	0.739
Weight (kg)	87.5 (75.0–98.0)	88.0 (79.0–98.0)	0.732
First systolic BP (mmHg)	151.0 (135.0–162.0)	155.0 (145.0–163.0)	0.126
First diastolic BP (mmHg)	108.0 (97.0–117.0)	109.0 (97.0–116.0)	0.362
BAI score	26.0 (25.0–37.0)	28.0 (25.0–32.0)	0.066

BAI: Beck Anxiety Inventory; BP: Blood pressure; SSRI: Selective serotonin reuptake inhibitor. Data are presented as median (min-max). Mann–Whitney U-test.

and last diastolic BP, and diastolic BP difference, while no relationship was found between systolic BP difference (respectively, r=0.342 and p=0.001; r=0.235 and p=0.025; r=0.517 and p<0.001; r=0.264 and p=0.011; r=0.339 and p=0.001; p>0.05). The relationship between BP measurements is summarized in Table 2.

DISCUSSION

This study aimed to investigate the effect of SSRI group drugs on BP control in resistant HT patients with anxiety symptoms. The findings of the study show that SSRI treatment provides significant reductions in both systolic and diastolic BP. These findings support the potential role of SSRI treatment in alleviating the negative effects of anxiety on BP control in patients with anxiety symptoms.

Anxiety is an important psychosocial factor that attracts attention in HT management because of its effects on BP.[8,9] Anxiety causes activation of the sympathetic nervous system in the body and thus increased cardiac output and peripheral vascular resistance, and anxious individuals often struggle with behavioral factors, such as low medication adherence and unhealthy lifestyle preferences.[5,7] Unfortunately, this situation poses a challenge to clinicians in the management of HT. Every clinician should consider these difficulties and possible treatments in HT management.[10]

The findings of this study are compatible with the existing literature examining the relationship between anxiety and HT. Especially in recent meta-analyses and reviews, this relationship has been emphasized.[11-13] For example, the results of the meta-analysis conducted by Pan et al., in 2015 including 151,389 patients, revealed that anxiety increased the risk of HT and emphasized the importance of early detection and management of anxiety in hypertensive patients.[14] In this study, it was observed that patients with anxiety symptoms had difficulty in BP control, and SSRI treatment improved BP control in these patients.

Table 2. The relationship between BP measurements

	First systolic BP (mmHg)	Last systolic BP (mmHg)	Δ Systolic BP (mmHg)	First diastolic BP (mmHg)	Last diastolic BP (mmHg)	Δ Diastolic BP (mmHg)
First systolic BP (mmHg)	1	r=0.787	r=0.289	r=0.484	r=0.478	r=0.102
		p<0.001	p=0.005	p<0.001	p<0.001	p=0.338
Last systolic BP (mmHg)		1	r=−0.278	r=0.413	r=0.521	r=−0.132
			p=0.008	p<0.001	p<0.001	p=0.212
Systolic BP (mmHg)			1	r=0.057	r=−0.083	r=0.315
				p=0.593	p=0.432	p=0.002
First diastolic BP (mmHg)				1	r=0.684	r=0.479
					p<0.001	p<0.001
Last diastolic BP (mmHg)					1	r=−0.247
						p=0.018
Diastolic BP (mmHg)						1

BP: Blood pressure; Spearman correlation test.

When the literature is reviewed, unfortunately, it is seen that the diagnosis and treatment processes of diseases, such as HT are not sufficiently covered in medical education. However, the etiological questioning of HT, which is seen with a high frequency in society, should be done very well. The findings of this study show that in refractory HT patients in whom the possibility of secondary HT is excluded, the accompanying psychological comorbidities of the patient should be questioned.[15] The findings of this study emphasize the importance of questioning the psychological status of HT patients and developing treatment strategies for selected patients, and including this in medical education. In this respect, this present study, with its prospective nature, is a study that questions the effects of SSRIs on BP in patients with refractory HT and anxiety disorders and can make important contributions to the literature in the field.

This study has some limitations. The limited number of participants, the fact that the data were collected from a single center, and the relatively short follow-up period limit the generalizability of the results. In addition, although SSRI treatment was recommended for all patients, the presence of groups that accepted and did not accept treatment based on patient preference may have affected the study results. Prospective studies with larger sample sizes and longer follow-up periods are needed.

CONCLUSION

In patients with refractory HT, the accompanying psychological comorbidities of the patients should be questioned. The findings of this study emphasize the importance of questioning the psychological status of patients with HT and developing treatment strategies for selected patients. SSRI treatment may improve BP control in resistant HT patients with anxiety symptoms, and these findings should be considered in clinical practice.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: There is no conflict of interest between the authors or family members of the authors. The authors do not have any consultancy, expertise, working conditions, shareholding, or similar situations that may lead to potential conflicts of interest in any company.

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Ethics Committee Approval: Approval for the study was obtained from the Health Sciences University Trabzon Medical Faculty Clinical Research Ethics Committee (Approval date: 25.10.2023, Approval number: 2023-7). Verbal and written informed consent were obtained from all participants before the study and the principles of the Declaration of Helsinki, as revised, were followed at every stage of the study.

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