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Original Article

Cerebellin and Catecholamines in Newly Diagnosed Hypertension With and Without Diabetes Mellitus

Diabetes Mellitus Olan ve Olmayan Yeni Tanı Hipertansiyonda Serebellin ve Katekolamin Düzeyleri

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ABSTRACT

Objective: The combination of diabetes mellitus and hypertension accelerates vascular complications and increases the risk of mortality and morbidity. The association of hypertension and diabetes mellitus is due to the common mechanism responsible for the pathogenesis of both diseases. The current study aimed to determine how catecholamine and cerebellin levels were affected both before and after treatment in the urine and blood of patients with hypertension and hypertension + diabetes mellitus.

Methods: This cross-sectional study included 30 patients with newly diagnosed hypertension, 30 patients with previously diagnosed diabetes mellitus and new hypertension, and 30 healthy controls. Serum and urinary levels of cerebelline, adrenaline, noradrenaline, metanephrine, and normetanephrines were measured by ELISA. Other biochemical parameters (Fasting Blood Glucose [FBG], glycosylated hemoglobin A, low-density lipoprotein, and triglyceride) were measured by autoanalyzer. In addition, the clinical characteristics of the collected patients were also recorded including age, gender, blood pressure, and body mass index.

Results: The gender was similar among the control, hypertension, and hypertension + diabetes mellitus groups ($P > .05$). There was a significant decrease in blood and urine cerebellin, metanephrine, and normetanephrine levels in hypertension + diabetes mellitus patients compared with both newly diagnosed

ÖZ

Amaç: Diabetes mellitus ve hipertansiyon kombinasyonu vasküler komplikasyonları hızlandırır ve mortalite ve morbidite riskini artırır. Hipertansiyon ve diabetes mellitus ilişkisi, her iki hastalığın patogenezinden sorumlu ortak mekanizmadan kaynaklanmaktadır. Bu çalışmada hipertansiyon ve hipertansiyon+diabetes mellituslu hastaların idrar ve kanlarında tedavi öncesi ve sonrasında katekolamin ve serebellin düzeylerinin nasıl etkilendiğinin belirlenmesi amaçlandı.

Yöntemler: Bu kesitsel çalışmaya diyabeti olmayan yeni tanı konmuş 30 hipertansiyon hastası, önceden diyabetes mellitus ve yeni hipertansiyon tanısı almış 30 hasta ve 30 sağlıklı kontrol alındı. Serebellin, adrenalin, noradrenalin, metanefrin ve normetanefrin serum ve idrar seviyeleri ELISA yöntemi ile ölçüldü. Diğer biyokimyasal parametreler (açlık kan şekeri, HbA1c, LDL, trigliserit) otoanalizör ile ölçüldü. Ek olarak, hastaların yaş, cinsiyet, kan basıncı ve beden kitle indeksleri kaydedildi.

Bulgular: Cinsiyet açısından gruplar arasında anlamlı farklılık yoktu ($P > .05$). Hipertansiyon+diabetes mellitus hastalarında kan ve idrar serebellin, metanefrin ve normetanefrin düzeylerinde hem yeni tanı hipertansiflere hem de kontrollere göre anlamlı azalma oldu ($P < .001$). Yeni tanı konan hipertansiyon ve kontroller arasındaki serebellin düzeyleri açısından fark yoktu ($P=.395$). Serebellin ile sistolik ve diyastolik kan basıncı ve adrenalin arasında anlamlı bir negatif korelasyon vardı.

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hypertension and controls ($P < .001$). There was no difference in cerebellin levels between newly diagnosed hypertension and controls ($P = .395$). There was a significant negative correlation between cerebellin and systolic and diastolic blood pressure and adrenaline.

Conclusion: This result suggests that there is a relationship between cerebellin, catecholamine, and catecholamine metabolites in hypertension and hypertension + diabetes mellitus patients. In the future, there is a need for further studies on the possibility that these biomarkers can give an idea about the etiopathogenesis of diseases such as hypertension and diabetes mellitus.

Keywords: Adrenaline, blood pressure, cerebellin, diabetes mellitus, epinephrine, hypertension, normetanephrine

Sonuç: Mevcut bulgular hipertansiyon ve hipertansiyon+diabetes mellitusta serebellin, katekolamin ve katekolamin metabolitleri arasında ilişki olduğunu düşündürmektedir. Bu biyobelirteçlerin hipertansiyon ve diyabetes mellitus etiyopatogenezindeki rolünün anlaşılması için daha fazla çalışmaya ihtiyaç vardır

Anahtar Kelimeler: Adrenalin, kan basıncı, serebellin, diyabetes mellitus, epinefrin, hipertansiyon, normetanefrin.

INTRODUCTION

Hypertension is currently the most important risk factor for cardiovascular diseases. Hypertension (HT), which has a high prevalence, is observed with a frequency of approximately 30% in the adult population. The prevalence of HT increases significantly with age. Due to this feature, it makes a significant contribution to morbidity and mortality worldwide and creates a great socioeconomic burden. Despite great progress in awareness, diagnosis, and treatment of HT today, unfortunately, less than half of hypertensive patients can have blood pressure under control. Diabetes mellitus (DM) is another important cardiovascular risk factor that is common worldwide, such as hypertension. The coexistence of high blood pressure and diabetes is very common. While the vascular and renal effects of DM cause an increase in blood pressure, the deterioration of carbohydrate metabolism in hypertensive individuals has been shown to be the reason for this association.[1]

Chronic diseases such as DM accompanying HT make blood pressure control difficult. Blood pressure control can be achieved in only 29.6% of hypertensive individuals. However, the most important factor in reducing cardiovascular diseases is lowering blood pressure. Reducing blood pressure by just 10 mmHg can reduce diabetic complications and death from diabetes and cardiovascular disease.[2]

MAIN POINTS

- Catecholamines were significantly higher in both newly diagnosed hypertensive patients and diabetic hypertensive patients than in controls.
- Cerebellin levels were significantly lower in diabetic hypertensive patients than in both newly diagnosed hypertensive patients without type 2 diabetes mellitus (T2DM) and controls.
- Low cerebellin may play a role in the coexistence of T2DM and hypertension.

Catecholamines (adrenaline, noradrenaline, and dopamine) mediate various biological effects in organs and tissues through adrenergic receptors. Catecholamines cause vasoconstriction by activation of α1-receptors and positive inotropic and chronotropic effects in the heart by activation of β1-receptors, causing tachycardia and HT. Due to this mechanism of action, it has been assumed that the increase in sympathetic adrenomedular activity plays a role in the formation of HT.[3,4] Previous studies have reported an increase in noradrenaline levels in one-third of hypertensive individuals. In another study, it was reported that adrenaline infusion increased blood pressure, but this was temporary, and catecholamines had no effect on chronic blood pressure elevation and HT. It has been shown that in patients with pheochromocytoma, only catecholamine levels increase, blood pressure increases during attacks, and blood pressure is controlled with pheochromocytoma treatment.[5]

Findings that cerebelline increases the secretion of aldosterone, cortisol, and catecholamine brought to mind the possible role of cerebelline in the etiology of HT and DM. As with pheochromocytoma, cerebellin may cause increased blood pressure through catecholamine secretion.[6] In addition, cerebellin has been reported to have inhibitory effects on insulin and plasma thyroid-stimulating hormone secretion and stimulatory effects on neuropeptide Y secretion from the hypothalamus. Through this effect, it may play a role in the etiology of DM.[7]

In the light of the mechanisms described above and previous literature data, it was thought that serum cerebellin levels also play a role in DM and blood pressure regulation. Studies examining cerebellin levels in hypertensive and diabetic hypertensive individuals are limited. Investigation of the relationship between cerebellin and blood pressure may contribute to effective blood pressure control in HT and diabetic patients, which are the most important cardiovascular disease risk. The current study aimed to investigate the relationship between serum cerebellin

and catecholamine levels and blood pressure in hypertensive patients with and without DM.

METHODS

Study Design and Patients

This cross-sectional study was conducted in the internal medicine clinic of a tertiary university hospital between May 2017 and June 2018. The study included 30 newly diagnosed hypertensive patients, 30 patients with known type 2 diabetes (T2DM) and newly diagnosed hypertension, and 30 sex-matched healthy controls. Exclusion criteria of the study are as follows: type 1 DM, pregnancy, endocrine disorders other than DM, pheochromocytoma, malignancies, chronic kidney failure, substance abuse, acute infections, and heart failure.

The diagnoses of HT and DM were confirmed by internal medicine specialist. The newly diagnosed hypertensive patient group included in the study was composed of participants without a known history of HT and who were diagnosed with HT as a result of their follow-up in the last 3 months in our clinic. In the study, the diagnosis of HT was confirmed by considering office blood pressure measurements. By using appropriate measurement methods, threshold blood pressure value of 140/90 mmHg and above was accepted as HT in repeated office blood pressure measurements. Patients with a known diagnosis of T2DM and meeting the criteria for diagnosis of HT in their follow-up constituted the T2DM and newly diagnosed HT patient group. All of the patients included in this group were followed up in our clinic with the diagnosis of T2DM. Patients with a known diagnosis of T2DM and meeting the criteria for diagnosis of HT in their follow-up constituted the T2DM and newly diagnosed HT patient group. The diagnosis criteria of T2DM in our clinic are as follows: fasting plasma glucose level ≥126 mg/dL, oral glucose tolerance test second hour plasma glucose level ≥200 mg/dL, glycosylated hemoglobin A (HbA1c) ≥ 6.5%, or random plasma glucose level ≥200 mg/dL accompanying diabetes symptoms. At least 1 criterion was sufficient for the diagnosis of DM.[8]

Data Collection

The age, gender, height, and weight of the participants were recorded in the data collection tools. Height and weight of all participants were measured with a regularly calibrated scale and height meter. Fasting blood samples were taken from all participants for routine biochemical parameters (glucose, total cholesterol, low-density lipoprotein, triglyceride, HbA1c) and sent to the laboratory. All biochemical analyses were done in the same biochemistry laboratory using an automated biochemical analyzer (FUJI DRI-CHEM 4000i, Fuji, Japan). In the study, blood and urine samples were taken for the measurement of catecholamine and cerebellin levels. After centrifugation, these samples were stored at −80°C until the experiment date. Antihypertensive treatment (Angiotensin-converting enzyme [ACE] inhibitor and calcium channel blocker combination) was started in newly diagnosed hypertensive and hypertensive diabetic patient groups included in the study. Blood and urine samples were taken again on the 30th day of the treatment from the group in which the treatment was started. After these samples were centrifuged again, they were stored at −80°C until the day of analysis.

Analyses of the Catecholamine and Cerebellin

In the study, serum metanephrine levels were studied using the Human Metanephrine (MN) ELISA Kit catalog no: OPH1F1178 (Optima Medical and Kimyevi Maddeler Tic. Ltd. Şti., Istanbul, Turkey), serum norepinephrine levels were studied using the Human Norepinephrine (NE) ELISA Kit catalog no: OPH1F2001 (Optima Medical and Kimyevi Maddeler Tic. Ltd. Şti.), serum epinephrine/adrenaline levels were studied using the Human Epine phrine/Adrenaline, EPI ELISA Kit catalog no: OPH1F0668 (Optima Medical and Chemical Substances Tic. Ltd. Sti.), serum cerebellin levels were studied using the Human Cerebellin-1 CBLN1 ELISA Kit catalog no: OPH1F2642 (Optima Medical and Kimyevi Maddeler Tic. Ltd. Şti.), and serum normetanephrine levels were studied using the Human Normetanephrine NMN ELISA Kit catalog no: OPH1F2641 (Optima Medical and Kimyevi Maddeler Tic. Ltd. Şti.) using the ELISA method in accordance with the working procedures specified in the kit catalogs.

Statistical Analysis

Study data were analyzed with the Statistical Package for Social Sciences program for Windows version 22.0 (SPSS Inc., Chicago, Ill, USA). The normal distribution characteristics of the data were analyzed with the Shapiro–Wilk test. Categorical data were presented as frequency and percentage, and continuous variables as mean ± standard deviation (SD) or median (quartile 1-quartile 3). Pearson chi-square test was used to compare categorical data. In the comparison of continuous data, the one-way analysis of variance test was used for those with normal distribution, and the Kruskal–Wallis test for those with non-normal distribution. Bonferroni correction was used in pairwise comparisons. Spearman or Pearson correlation analysis tests were used for correlation analysis. A value of $P < .05$ was considered statistically significant.

RESULTS

A total of 90 participants were included in the study. The study groups were similar in terms of gender ($P = .549$). Systolic blood pressure (SBP), diastolic blood pressure (DBP), and body mass index were higher in hypertensive

Table 1. Demographic and Biochemical Characteristics of the Participants

Variables	Controls[1] n = 30	Newly HT[2] n = 30	T2DM+HT[3] n = 30	*P**	*P***
Gender (female/male)	20/10	22/8	18/12	.549[a]	
Age (year)	28.50 (21.50-36.50)	49.50 (37.50-64.25)	60.50 (55.00-68.50)	<.001[b]	1-2:<.001
					1-3:<.001
					2-3:.002
Glucose (mg/dL)	87.50 (81.00-91.25)	93.00 (87.75-97.25)	180.00 (126.25-216.25)	<.001	1-2:0.999
					1-3:<.001
					2-3:<.001
HbA1C (%)	4.50 (4.40-4.75)	4.60 (4.40-4.70)	7.20 (6.60-8.05)	<.001	1-2:0.999
					1-3:<.001
					2-3:<.001
LDL (mg/dL)	101.40±34.08	134.90 ± 34.68	131.13 ± 32.31	.001[c]	1-2:.002
					1-3:.006
					2-3:.999
Triglyceride (mg/dL)	91.00 (61.50-119.25)	117.00 (89.75-188.00)	150.00 (114.75-211.50)	<.001	1-2:.053
					1-3:.028
					2-3:.999
SBP (mm/Hg)	110.00 (100.00-120.00)	170.00 (158.75-170.00)	167.50 (159.50-176.25)	<.001	1-2:<.001
					1-3:.001
					2-3:.999
DBP (mm/Hg)	73.00 (70.00-80.00)	102.50 (94.25-110.00)	105.00 (95.00-115.00)	<.001	1-2:<.001
					1-3:<.001
					2-3:.999
BMI (kg/m^2)	25.13±4.69	28.35±5.19	29.66±5.47	.003	1-2:.041
					1-3:.003
					2-3:.981

BMI, body mass index; DBP, diastolic blood pressure; HT, hypertension; LDL, low-density lipoprotein; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus.
[a]Pearson chi-square test; [b]Kruskal–Wallis test; [c]One-way ANOVA test; *P* value*, multiple comparisons; *P* value**, binary comparisons.

and diabetic hypertensive participants than in controls ($P < .05$). Glucose and HbA1c levels were significantly higher in diabetic participants than in both hypertensive patients without diabetes mellitus and controls ($P < .05$) (Table 1).

Adrenaline levels were significantly higher in both newly diagnosed hypertensive patients and diabetic hypertensive patients than in controls ($P < .001$). Noradrenalin levels were significantly increased in newly diagnosed hypertensive patients than in diabetic hypertensive patients and controls ($P < .001$). Cerebellin levels were significantly lower in diabetic hypertensive patients than in both newly diagnosed hypertensive patients without T2DM and controls ($P < .001$). There was no significant cerebellin level difference between newly diagnosed hypertensive patients and controls ($P = .395$) (Table 2).

There was a significant negative correlation between cerebellin levels and SBP ($r = -0.340$, $P = .001$), DBP ($r = -0.359$, $P = .001$), and adrenaline levels ($r = -0.235$, $P = .026$). There was a positive correlation between cerebellin levels and metanephrine ($r = 0.509$, $P < .001$) and normetanephrine levels ($r = 0.718$, $P < .001$). There was no significant correlation between cerebellin levels and noradrenaline levels ($r = 0.196$, $P = .064$) (Table 3).

The current study investigated the effect of antihypertensive therapy on cerebellin and catecholamine levels in study groups. There was no significant difference

Table 2. Comparison of Baseline Catecholamine and Cerebellin Levels According to Groups

	Controls[1]	Newly HT[2]	T2DM + HT[3]		
Variables	**n = 30**	**n = 30**	**n = 30**	***P****	***P*** **
Adrenaline (serum)	81.75 (73.00-92.13)	132.50 (85.00-245.50)	161.00 (97.75-271.75)	***<.001***	1-2:<.001
					1-3:<.001
					2-3:.719
Adrenaline (urinary)	74.75 (67.00-87.13)	127.50 (73.88-200.88)	115.50 (70.88-196.00)	***.002***	1-2:.004
					1-3:.008
					2-3:>.999
Noradrenaline (serum)	188.50 (126.50-432.88)	981.75 (635.75-1324.75)	418.50 (287.63-635.50)	***<.001***	1-2:<.001
					1-3:.296
					2-3:.003
Noradrenaline (urinary)	130.50 (121.63-135.75)	836.25 (310.63-1114.13)	402.75 (302.13-504.50)	***<.001***	1-2: <.001
					1-3:<.001
					2-3: :.532
Metanephrine (serum)	31.75 (25.13-176.38)	31.75 (26.37-74.63)	24.50 (17.63-52.75)	***.015***	1-2:>.999
					1-3:.044
					2-3:.031
Metanephrine (urinary)	27.00 (23.00-34.00)	27.25 (24.37-34.00)	18.50 (15.37-27.50)	***.002***	1-2: >.999
					1-3:.006
					2-3:.007
Normetanephrine (serum)	44.50 (15.88-206.75)	34.75 (25.13-53.38)	12.00 (8.00-20.75)	***<.001***	1-2:>.999
					1-3:<.001
					2-3:<.001
Normetanephrine (urinary)	24.25 (18.13-33.75)	28.00 (16.38-41.50)	10.75 (8.88-12.63)	***<.001***	1-2:>.999
					1-3:<.001
					2-3:<.001
Cerebellin (serum)	1301.75 (884.00-3035.25)	1196.00 (863.00-1934.13)	268.08 (127.38-422.13)	***<.001***	1-2: .395
					1-3:<.001
					2-3:<.001
Cerebellin (urinary)	972.50 (820.50-1282.88)	944.75 (607.75-1186.25)	251.75 (148.25-334.63)	***<.001***	1-2:.854
					1-3:<.001
					2-3:<.001

HT, hypertension; T2DM, type 2 diabetes mellitus.
***Kruskal–Wallis test; *P* value*, multiple comparisons; *P* value**, binary comparisons.

between baseline and after-treatment cerebellin and catecholamine levels in patients ($P > .05$) (Table 4).

DISCUSSION

The current study investigated the serum and urinary cerebellin levels in newly diagnosed hypertensive patients and type 2 diabetics who had newly diagnosed hypertension. In addition, catecholamine levels were also included in the study as a confounding factor, based on the hypothesis that catecholamines cause high blood pressure by activating the sympathetic system and that cerebelline can affect high blood pressure by increasing catecholamine secretion. The current study found that serum and urinary cerebellin levels significantly decreased in type 2 diabetics who had newly diagnosed hypertension than in newly diagnosed hypertension and controls. There was no significant difference between newly diagnosed hypertension patients and control.

Table 3. Correlation Between Cerebellin Level with Blood Pressure and Catecholamines

Variables	Serum Cerebelline	Variables	Urinary Cerebellin
SBP	*r*: −0.340; ***P: .001***	SBP	*r*: −0.426; ***P < .001***
DBP	*r*: −0.359; ***P: .001***	DBP	*r*: −0.390; ***P < .001***
Adrenaline (serum)	*r*: −0.235; ***P: .026***	Adrenaline (urinary)	*r*: −0.330; ***P: .001***
Noradrenaline (serum)	*r*: 0.196; *P: .064*	Noradrenaline (urinary)	*r*: −0.264; ***P: .012***
Metanephrine (serum)	*r*: 0.509; ***P < .001***	Metanephrine (urinary)	*r*: 0.405; ***P < .001***
Normetanephrine (serum)	*r*: 0.718; ***P < .001***	Normetanephrine (urinary)	*r*: 0.537; ***P < .001***

DBP, diastolic blood pressure; SBP, systolic blood pressure.

In the current study, adrenaline and noradrenaline levels were found to be higher in hypertensive and diabetic hypertensive individuals compared to the control group. It is known that catecholamines cause an increase in blood pressure by stimulating the sympathetic nervous system.[3] Although it is accepted in the literature that catecholamines cause blood pressure to increase generally, the hypothesis of increased catecholamines in the etiology of hypertension is not universal. Despite studies showing that renal venous norepinephrine levels are increased in hypertensive patients,[9] another study also showed that norepinephrine levels do not increase.[10] Previous studies have reported that blood pressure increases in cases of increased catecholamine levels, such as pheochromocytoma, but this is not associated with chronic hypertension.[5] Although high catecholamine levels are associated with the development of hypertension in the literature, it has been reported that norepinephrine levels do not change between hypertensive and normotensive individuals. Seamon[5] reported that there was no difference between catecholamine levels of normotensive and hypertensive individuals, and neither plasma nor urine catecholamine levels were predictive for the diagnosis of hypertension. The current study was conducted among

Table 4. Comparison of Catecholamine and Cerebellin Levels Before and After Treatment

Participants	Variables	Baseline	After Treatment	*P*
HT	Adrenaline (serum)	132.50 (85.00-245.50)	103.25 (76.25-203.13)	.245
	Adrenaline (urinary)	127.50 (73.88-200.88)	116.25 (75.88-202.38)	.854
	Noradrenaline (serum)	981.75 (635.75-1324.75)	854.00 (475.88-1145.38)	.153
	Noradrenaline (urinary)	836.25 (310.63-1114.13)	825.00 (214.88-956.75)	.261
	Metanephrine (serum)	31.75 (26.37-74.63)	35.75 (23.88-62.13)	.180
	Metanephrine (urinary)	27.25 (24.37-34.00)	27.50 (24.75-33.75)	.502
	Normetanephrine (serum)	34.75 (25.13-53.38)	31.25 (22.50-41.13)	.111
	Normetanephrine (urinary)	28.00 (16.38-41.50)	30.50 (22.38-35.75)	.781
	Cerebelline (serum)	1196.00 (863.00-1934.13)	1294.50 (924.75-2368.25)	.629
	Cerebelline (urinary)	944.75 (607.75-1186.25)	936.00 (698.88-1061.75)	.845
T2DM+HT	Adrenaline (serum)	161.00 (97.75-271.75)	132.00 (98.13-194.25)	.147
	Adrenaline (urinary)	115.50 (70.88-196.00)	136.75 (87.25-167.25)	.465
	Noradrenaline (serum)	418.50 (287.63-635.50)	448.75 (262.63-525.25)	.349
	Noradrenaline (urinary)	402.75 (302.13-504.50)	389.00 (248.50-569.00)	.975
	Metanephrine (serum)	24.50 (17.63-52.75)	22.25 (15.50-33.50)	.572
	Metanephrine (urinary)	18.50 (15.37-27.50)	22.50 (15.87-33.75)	.279
	Normetanephrine (serum)	12.00 (8.00-20.75)	11.75 (8.88-16.13)	.432
	Normetanephrine (urinary)	10.75 (8.88-12.63)	10.25 (8.38-14.50)	.452
	Cerebelline (serum)	268.08 (127.38-422.13)	324.00 (243.60-383.25)	.491
	Cerebelline (urinary)	251.75 (148.25-334.63)	301.00 (158.25-345.63)	.586

HT, hypertension; T2DM, type 2 diabetes mellitus.

newly diagnosed hypertensive individuals and supported previous findings linking the development of hypertension with elevated catecholamine levels.[11,12]

The current study showed that cerebellin levels were lower in diabetic hypertensives compared to both newly diagnosed hypertensives and controls. Cerebellin levels did not differ between newly diagnosed hypertensives and the healthy controls. A previous study has reported that cerebellin has stimulated the secretion of aldosterone, cortisol, and catecholamine from the adrenal glands and may cause an increase in blood pressure by this mechanism.[13] This hypothesis support that increased cerebellin levels may play a role in the pathophysiology in newly diagnosed hypertensive individuals, but no difference was found between the newly diagnosed hypertensive and control groups in the current study. Previous studies reported that there were no differences in cerebellin levels between both primary hypertensive patients and preeclamptic patients than the healthy controls.[14,15] These findings were similar to the current study data. Cerebellin levels were found to be lower in diabetic hypertensives in the current study. Previous literature findings have reported that cerebellin levels may increase blood pressure due to the increase in catecholamines, but it has no role in the etiology of chronic hypertension.[5] Cerebellin may have increased both blood pressure and blood glucose with an increase in catecholamine levels. Increased blood glucose may have suppressed cerebellin levels with negative feedback. The reason for the difference in cerebellin levels between newly diagnosed hypertensive and diabetic hypertensive may be the negative feedback mechanism.

The current study showed that there was a negative correlation between cerebellin levels and SBP and DBP and adrenaline levels. Previous literature findings suggested that cerebellin causes an increase in blood pressure through an increase in catecholamines.[6,7] Current findings contradictory this hypothesis which is that cerebellin increase causes catecholamine increase. There was no significant correlation between cerebellin and noradrenaline. Studies examining the level of cerebellin in patients diagnosed with hypertension are very limited in the literature. As mentioned above, increased blood pressure and blood glucose can cause suppression of cerebellin levels with negative feedback. In the current study, cerebellin and catecholamine levels were investigated in patients again after antihypertensive treatment. There was no difference between pre- and post-treatment catecholamine and cerebellin levels. Performing post-treatment control analyses on the 15th day may be insufficient to evaluate the time required for negative feedback and reduction of cerebellin. There is no study in the literature examining the level of cerebellin after antihypertensive treatment. The current study is also insufficient to explain the relationship between antihypertensive treatment and cerebellin. We believe that new studies are needed to elucidate the relationship between cerebellin and antihypertensive treatment.

The first possible limitation of the study was that it was cross-sectional and conducted in a narrow population. Control blood analyses were assessed on the 15th day of treatment and it may have limited the evaluation of the effectiveness of the antihypertensive treatment. We thought that there is a need for new studies in which patient follow-up can be carried out for a longer period of time. The significant difference between the median age values of the groups is another limitation. The age of the participants may have influenced the results. In future studies, there is a need for results to be obtained with subjects in the similar age range. It was thought that randomized controlled studies with large populations, including patients in the pre-hypertensive period, are needed for showing the role of cerebellin in the etiology of hypertension

In conclusion, cerebellin levels were decreased in patients with type 2 diabetes who had newly diagnosed hypertension. There was no difference in cerebellin levels between patients with newly diagnosed hypertension and controls. In the future, there is a need for further studies on the possibility that cerebellin and catecholamines can give an idea about the etiopathogenesis of diseases such as HT DM.

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Fırat University (Date: April 20, 2017, Decision No: 07/15).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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