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Association of Apelin and Nitrous Oxide with Essential Hypertensive Patients and their Relation to Sex

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Abstract

Apelin is a new multi-functional peptide that has already been linked to blood pressure and cardiac function modulation. It's hypothesized to play a role in hypertension and hypertensive heart diseases development., Nitric oxide (NO) was recognized as an endogenous signaling molecule that modulates vascular compliance and organ perfusion via its powerful vasodilatory effects. Hypertension, atherosclerosis, and chronic renal problems are hypothesized to limit nitric oxide bioavailability, leading to disease progression. Our study aimed to know the role of apelin and nitric oxide in the pathogenesis of essential hypertension and correlate the levels of apelin to nitric oxide in both genders, A total number of 90 participants (70 hypertensive patients and 20 control) were enrolled, and all participants underwent blood pressure, serum apelin and nitric oxide measurement, our results revealed decreased serum apelin levels in essential hypertensive patients, while serum nitric oxide was increased compared to controls with no significant gender difference.

Keywords: Apelin, Nitic Oxide, Hypertension

Introduction

Essential hypertension is a significant risk factor for a variety of comorbidities, including cerebrovascular diseases, coronary artery diseases, heart failure, and chronic kidney disease [(1).] Hypertension is one of the most frequent complicated illnesses. The etiology of hypertension varies greatly among individuals within a large population, and essential hypertension has no recognized cause. However, various risk factors have been found[(2)]. In the vascular endothelium, several hormones, humeral vasoactive peptides, growth, and regulatory peptides are generated, such as apelin and NO. Apelin is a new multi-functional peptide that has already been linked to blood pressure and cardiac function modulation. It's hypothesized to play a role in hypertension and hypertensive heart disea-

se development. There are at least three different types of apelin. Each of these proteins has 13, 17, or 36 amino acids and is generated from a 77-amino-acid precursor [3]. Apelin promotes endothelial-dependent, nitric oxide-mediated vasorelaxation and reduces arterial blood pressure. Furthermore, Apelin has a potent and long-lasting favorable inotropic effect that persists even in injured myocardium and is not followed by cardiac hypertrophy [4, 5].

Aside from controlling cardiovascular function, apelin also prevents water intake and suppresses the production of vasopressin. As a result, think of a novel agent for influencing cardiovascular function. By activating the G-protein–coupled receptor, apelin contributes to the physiology and pathophysiology of the cardiovascular system [3], apelin promotes diuresis by antagonizing arginine vasopressin and has a beneficial inotropic impact on the heart by causing vasodilation with consequent blood pressure reduction via a NO-dependent mechanism [6].

The function of the cholinergic system in hypertension, with its hemodynamic variations and cardiac issues, maybe an exciting area of study; nevertheless, the function of the cholinergic system in this entity has not yet been thoroughly investigated. Indeed, apelin levels in hypertension patients were significantly lower than in controls, and hypertensive patients without concomitant diseases affecting cardiovascular functions had lower serum apelin levels than controls [7].

Nitric oxide was recognized as an endogenous signaling molecule that modulates vascular compliance and organ perfusion via its powerful vasodilatory effects. NO is generated by the enzyme nitric oxide synthase (NOS) and is currently recognized to have a key role in a range of biological activities, including sympathetic activity modulation in vasomotor centers, vascular smooth muscle contraction, sodium excretion by the kidney, renin secretion, and extracellular volume preservation [8]. Some chronic diseases, such as DM, essential hypertension, IHD, and CKD, are hypothesized to limit NO bioavailability, leading to disease progression [9].

Endothelial dysfunction, which is distinguished by decreased NO bioavailability, is a significant predictor of both hypertension and cardiovascular disease and may be a crucial link between these two illnesses. Evidence shows that NO plays a significant role in blood pressure regulation and that decreased NO bioactivity is a key element of hypertension. Clinical investingations have revealed that hypertensive individuals have a decreased arterial vasodilator response to endothelium-dependent vasodilators and that NOS inhibition elevates blood pressure [10].

Our study aimed to know the role of apelin and nitric oxide in the pathogenesis of essential hypertension and correlate the levels of apelin to nitric oxide in both genders.

Patients and methods

Study group:

This study was performed at Sohag University Hospital, The study enlisted the participation of 70 patients. 20 normotensive groups were matched on age, BMI, and sex ratio. A sphygmomanometer was used to measure blood pressure in the right arm, after a 15-minute rest period, all measures were taken in the supine position. Results were the average of measurements obtained on at least 3 separate days. If the systolic blood pressure was equal to or greater than 140 mmHg or the diastolic blood pressure was equal to or greater than 90 mmHg, or if the patient reported taking blood pressure medication, hypertension was considered. The study was approved

by the Ethical Committee of the Sohag Faculty of Medicine and informed written consent was obtained from all subjects included in the study.

Samples collection and laboratory investigation:

Overnight fasting blood samples (about 5 ml) were taken from the patients and controls in sterile tubes through venipuncture of an antecubital vein. The serum was extracted from the samples and centrifuged at 3000 rpm to determine NO and apelin levels. Apelin was measured by an ELIZA test kit supplied by WKEA MED SUPPLIES CROP (code NO: WH-1717).

- NO was measured using a colorimetric nitrite/nitrate assay kit supplied by Cayman chemicals (Cat.No.:E-BC-K070-S).

Statistical analysis

The results were presented as means standard deviations. The Mann-Whitney test was used to evaluate continuous data, while the Chi-Square test was used to assess categorical data. Significant P-values were defined as those less than 0.05. To assess the link between the parameters, the Pearson correlation test was used. SPSS (Statistical Package for the Social Science; SPSS, Chicago, IL, USA) version 16 for Microsoft Windows, USA was used to do all statistical computations.

RESULTS

The study's findings indicated that the patients and controls were age, sex distribution, and BMI matched (P>0.05). When hypertension patients were compared to controls, there was a substantial difference in systolic blood pressure (SBP), a significant drop in apelin, and a significant rise in NO, ***table (1)***.

Table (1): Clinical and laboratory characteristics of the participants.

	Controls (n=20) Mean ± SD	Patients (n=70) Mean ± SD	p-value
age	54.8 ± 11.97	58.77±9.82	0.191
Male/female	10/10	38/32	0.736
BMI	21.55 ± 2.04	21.18 ± 2.183	0.563
sBP(mmHg)	121 ± 6.996	158.7 ± 17.83***	< 0.0001
dBP(mmHg)	77.50 ± 6 .98	80.36 ± 7.19	0.1183
NO (µmol/l)	18.77 ± 1.353	27.98 ± 6.6	0.001
Apelin (ng/L)	1616 ± 940	1070 ± 465	< 0.0001

BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, NO: Nitrous oxide

Using the Independent student t-test, the difference between males and females in apelin, NO in both genders was determined. ***table (2)*** there is no significant difference between both sexes regarding apelin or NO as the p-value was (0.935) in apelin and (0.167) in Nitrous oxide.

Table (2) independent sample t-test comparing apelin, Nitrous oxide in both gender.

	Apelin (ng/L)		Nitrous oxide (µmol/l)	
	Male	Female	Male	Female
Mean	1026.30	1008.73	28.53	27.52
±SD	491.57	448.25	7.42	5.88
Mean difference	17.57		1.007	
t value	0.156		0.633	
p value	0.935		0.167	
Significance.	N.S.		N.S.	

SD: standard deviation, N.S: Non-significant

The correlation between Blood Pressure, Nitrous oxide, and apelin is shown in ***Table (3)***, the correlation coefficient value between Blood Pressure and age was (-0.158 and -0.036), which means a non-significant Negative correlation as p-value >0.05. While the correlation coefficient value between Blood Pressure and Nitrous oxide was 0.752 which means a significant positive correlation with a p-value <0.001. Although the correlation coefficient value between Blood Pressure and apelin was -0.55 which means a significant negative correlation as p-value <0.001

Table (3): Correlation between the Blood Pressure and other variables in both groups.

CORRELATION		Age	Apelin	Nitrous oxide
B.P.	r-value	-0.158	-0.550	0.752
	P-value	0.138	0.001	0.001
	Level of significance	N.S.	S.	S.

B.P: blood pressure, N.S: non significant, S:significant , P value >0.005 is non significan, P value <0.005 is significant

Discussion

In our study, when compared to controls, serum apelin levels in essential hypertensive patients were found to be significantly lower, a result similar to those found by other studies [11-13]. Apelin is a multifunctional peptide that was reported to have a role in the regulation of the cardiovascular system and to be involved in the pathophysiology of hypertension. chronic application of apelin to deoxycorticosterone acetate-salt-induced hypertensive rats (DOCA-salt rats) reduces blood pressure [14]. The Apelin receptor (APJ) was discovered to play a function in a G-protein-independent and the β-arrestin-dependent manner in modulating the stretch response inside the heart [15].

NO levels were observed to be higher in essential hypertension patients compared to controls in this work. Other reports postulated that NO positively correlated to systolic and diastolic blood pressure[10,16,17], in addition, spontaneously hypertensive rats exhibited an increase in NO synthesis in vascular smooth muscle cells [18]. The increase in NO levels can be attributed to the medications that the hypertensive patients received, as most patients receive angiotensin-conve-

rting enzyme inhibitors which improve endothelial function, increasing NO synthesis[19]. The negative association between apelin and serum electrolytes could be explained based on the fact that apelin serves as a catalytic substrate for angiotensin-converting enzyme 2 and functions as an inotropic and cardioprotective peptide [20]. The Apelin/APJ system is involved in a wide range of pathophysiological processes in the cardiovascular system, thus playing a role in the initiation and development of various cardiovascular diseases like pulmonary and essential hypertension [21]. Apelin levels were lowered in individuals with essential hypertension, regardless of systolic or diastolic dysfunction in the left ventricle [22] and treatment with apelin re-duced systolic blood pressure in hypertensive rats through NO-dependent signaling [23]. In this study, we did not find any relation between apelin and NO on one side and sex on the other side as mentioned by other studies [24].

In conclusion, this study revealed decreased serum apelin levels in essential hypertensive patients, while serum NO was increased compared to controls. Apelin may impact blood hemostasis and so have a role in the pathophysiology of essential hypertension. However, further research is required to determine the precise mechanism through which apelin influences blood hemostasis.

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