Rize Medical Journal

Rize Medical Journal 2024;1(1):1-8

Clinical Research

Blood Apelin-36 Level in Patients with Depression

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Anahtar Kelimeler: Depression, Apelin, Mood Disorders
Başvuru Tarihi : 30.01.2024
Kabul Tarihi : 14.03.2024

Abstract

Aim: Major Depressive Disorder is an important health problem leading to significant disability. Biochemical parameters that can be used in the diagnosis and follow-up of Major Depressive Disorders severity are important for clinicians. The aim of our study was to investigate blood apelin levels in patients with Major Depressive Disorder as a marker for disease severity and diagnosis.

Materials and Methods: The study included 30 patients diagnosed with Major Depressive Disorder and 31 healthy controls. Hamilton Depression Scale was applied to the patient group. Blood apelin-36 levels were measured in both groups.

Results: Plasma apelin-36 level was 0.363±0.102 ng/ml (min-max: 0.173-0.611) in the patient group and 1.140±0.738 ng/ml (min-max: 0.323-2.547) in the healthy control group. Blood apelin-36 level of the patient group was statistically significantly lower than that of the healthy control group ($p<0.001$).

Conclusion: Blood apelin levels were found to be low in patients with Major Depressive Disorder. Apelin is an endogenous peptide with important physiological roles and looks promising as a biomarker. It's utility for the diagnosis and follow-up of mood disorders requires further investigation. In this respect, our research contributes to the literature.

Key Words: Depression, Apelin, Mood Disorders

Introduction

Apelin 36 is a novel endogenous peptide, which has an important physiological role[1]. It has been reported to be involved in cardiovascular function, fluid homeostasis, and modulation of immune response and pain[2-4]. It is expressed in the central nervous system in addition to peripheral tissues and cells such as hearth, kidney, lung and adipose[5].

Studies in rats have demonstrated that apelin 36 regulates hypothalamic-pituitary-adrenal (HPA) axis via a corticotrophin-releasing factor (CRF) and vasopressin (AVP)[6]. Boucher at al found that apelin 36 expression is markedly influenced by nutritional status in mice and humans and the authors suggested that hyper insulinemia and obesity may play a role in the regulation of apelin 36 Similarly, Heinonen et al showed that apelin levels in obese patients were significantly higher compared to controls and correlated positively with body muscle index (BMI)[7,8].

There is a lot of evidence for a direct involvement of impaired HPA axis in the etiology and symptoms of depressive disorder[9]. It has also been reported that alteration of food intake could affect stress sensitivity of HPA axis in depressive disorder[10]. Many studies have suggested that peptides such as ghrelin, nesfatin-1, leptin and neuropeptide Y might mediate the interaction between effect and appetite and induce stress-related behavior[11-14]. Telegdy and Jaszberenyi found that intra cerebro ventricular apelin injection led to anxiolytic action via α-adrenergic, dopaminergic, β-adrenergic and and 5-HT2 serotonergic mediation in mice[15].

Therefore, available evidence suggests that apelin 36 is involved in the pathophysiology of depression. The present study aims i) to investigate whether there is any difference between patients with Major Depressive Disorder (MDD) and controls in apelin 36 levels. ii) to determine the association of Hamilton Depression Scale (HAM-D) scores, BMI and apelin 36 level in MDD patients and controls.

Materials and Methods

The clinical protocol was approved by the local ethical committee. Consecutive patients with MDD who have attend the outpatient clinics of Department of Psychiatry, University Hospital, Rize, Turkey were enrolled. The control group comprised of healthy individuals matched with age and sex, and were selected from the community. Informed written consent was obtained from all participants. Demographic variables were recorded in a standardized interview. The BMI was calculated as body weight (kg) divided by the square of the height (m^2) (kg/m^2). The diagnosis of MDD was made based on the DSM-5 criteria by experienced psychiatry.

Patients who had any other comorbid psychiatric disorder and those with a history of inadequate cardiac function, renal dysfunction, diabetes, liver disease and cancer were excluded from the study. The severity of depressive symptoms was assessed using the HAM-D, validity and reliability studies of whose Turkish version have already been conducted[16]. The controls were matched for age and gender. The controls had no clinical psychiatric disorder. They had not taken any psychotropic drugs for at least two months prior to the study. Their psychiatric conditions were evaluated by the same psychiatrists in accordance with DSM-5. They had no past neurological, endocrinological, hepatic and renal diseases.

After blood collection for Apelin 36 measurement, serum was immediately obtained by centrifugation, transferred into cryotubes and stored at -70 °C until assayed. Serum Apelin 36 was measured using ELISA (AP36 test kit, Cloud-Clone Corp, Houston, USA) according to the manufacturer's protocol.

Statistical analysis was performed using SPSS 22. Mean ages were compared by Student's T Test; Pearson's Chi-Square Test was used to compare the gender between two groups. Normality assumptions of continuous variables were checked via Kolmogorov Simonov test. Student's T Test was employed to compare apelin 36 values between depressive patients and controls. Correlation analysis was performed by Spearman Correlation Coefficient test. Results were considered significant at $p<0.05$.

Results

The demographic and clinical characteristics of the patients and control groups were presented in **Table 1**. The groups did not differ in terms of age, sex and BMI (all $p>0.05$). The plasma apelin 36 level in patients with MDD was 0.363±0.102ng/ml (min-max:0.173-0.611), whereas it was 1.140±0.738ng/ml (min-max: 0.323-2.547) in the control group **(Table 1)**. Differences in plasma apelin 36 level between two groups was significant ($p<0.001$). The mean serum apelin 36 level did not show any correlation with age, HAM-D scores, and BMI in the patient group **(Table2)**.

Table 1. Demographic and clinical variables of patients and controls

	Patients (n=30)	Controls (n=31)	p
Age	32.87 ±5.16	31.83 ± 8.76	0.220
Gender (male/female)	11/19	14/17	0.500
BMI (kg/m²)	24.5±1.8	23.4±1.8	0.060
Duration of illness (years)	2.23±0.7	NA	NA
Apelin 36 level	0.363±0.102ng/ml	1.140±0.738ng/ml	<0.001*

BMI: Body Mass Index, NA: Not applicable, p<0.05

Table 2. Correlation analyses between apelin and other parameters in the patient and control groups

	Patients (n=30)		Controls (n=31)	
	Apelin		Apelin	
	r	p	r	p
Age	0.00	0.970	-0.14	0.430
BMI	0.09	0.630	0.10	0.560
HAM-D	0.06	0.750	NA	NA

BMI: Body Mass Index, HAM-D: Hamilton Depression Scale, NA: Not applicable, p<0.05

Discussion

In our study, the difference in blood apelin levels between the patient group and the healthy control group was analysed. The main finding of our study was that apelin 36 level in depressed patients is significantly lower compared to healthy controls. Several reasons may account for this finding. Central administration of the apelin 13 was demonstrated to play a role in regulation food intake[17]. A great deal of the literature has reported a close relationship between food intake and HPA axis function. This assumption is supported by the fact that many agents involved in appetite regulation such as nesfatin-1, orexin and ghrelin can affect HPA axis response to stress[18,19]. Involvement of these peptides in the pathophysiology of depression is suggested by numerous studies showing altered plasma concentrations[11,12,20]. In addition, abnormal HPA activity has been implicated in a variety of condition related to stress including depression and anxiety disorder[21]. The results of our as well as other studies imply that decreased apelin 13 may alter food intake through irregularities in HPA axis response to stress in depressed patients. Another issue to consider is that apelin receptors and apelin are widely distributed in the central nervous system and the neuroprotective effects of apelin have been well documented in rat studies. Apelin protect neurons from apoptosis and it blocks excessive NMDA receptor activation[5,22-25]. Previous studies demonstrated that reduction of neuronal

volume and neuronal loss occur in depression and decreased neuroprotective action may cause depressive disorder, effects that are counteracted by anti-depressants[26-28]. Plasma levels of neurotrophic factors such as BDNF and IGF-I decline in depressive disorder[29,30]. Together, it is probable that there may be direct or indirect relationship between depression and decline in the neuroprotective apelin.

No correlation between plasma apelin 36 level and HAM-D scores has been found in the patient group. It seems that apelin 36 levels are not correlated with the severity of disease.

There are some limitations in our study. The number of study participants is relatively low. In addition, this is a cross sectional study, evaluating only one time point for the measurement of apelin 36 levels.

Conclusion: Our results support the notion that apelin 36 may have a protective role in depression. Studies with larger groups and longitudinal follow-up are needed to justify these preliminary results.

Conflict of Interest: The authors declare that they have no competing interests.

Financial Disclosure: There is no specific funding related to this research

Ethics Committee Approval: Ethics committee approval of the study was obtained from Recep Tayyip Erdoğan University Non-İnterventional Ethics Committee (Ethics Committee No: 2022/56).

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