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Essential amino acids levels in individuals that attempted suicide

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ABSTRACT

Aims: In our study, plasma essential amino acid levels were analyzed in patients with depressed mood by comparing patients who applied to the emergency department after a suicide attempt with the control group. It was hypothesized that certain essential amino acid levels would be lower in individuals who attempted suicide compared to the control group.

Methods: Plasma/serum samples obtained from the control group and the patient group were removed from -80°C where they were stored and thawed, and all amino acid levels in plasma/serum were measured with Q-TOF LC/MS. Kolmogorov-Simirnov, Man-Whitney U test and Chi-square test were used in the evaluation of the data and the error level was taken as 0.05. In this study, $\alpha=0.05$; When $\beta=0.10$ and $(1-\beta)=0.90$, it was decided to include 35 individuals in each group and the power of the test was found to be $p=0.90744$.

Results: When the essential amino acids were examined in general, in the comparison made between the patient and control groups, methionine, leucine, isoleucine, valine, lysine, threonine, phenylalanine and tryptophan amino acids were found to be significantly low in the patient group ($p<0.05$). However, no statistically significant difference was found in the comparison made between the two groups for histidine amino acid ($p=0.405$; $p>0.05$).

Conclusion: In our study, it was concluded that suicidal behavior was more common in female gender and people with low socioeconomic status. Among the essential amino acids taken through nutrition, a significant decrease was found in this study, especially in amino acids that are precursors of important neurotransmitters (serotonin, noradrenaline, dopamine, etc.) that affect mood. At the same time, a significant decrease was found in amino acids that affect the skeletal-muscular system and play an active role in energy metabolism.

Keywords: Emergency medicine, food quality, amino acids, suicidal behavior

INTRODUCTION

Depression has become an important public health problem both individually and socially. In patients applying to health institutions, self-blame, worthlessness, hopelessness, and recurrent suicidal thoughts are at the forefront. Especially since physiological functionality is also impaired, loss of appetite, weight loss, sleep and concentration disorders, fatigue, psychomotor agitation, and retardation are observed in this patient population. Depression is considered a chronic process, and when left untreated, the number of attacks and destruction increases.[1]

Suicidal behavior has been one of the leading preventable causes of premature deaths that threaten life in recent years. Since emergency services are the first place patients apply and receive intervention after a suicide attempt, research on this population is gaining great importance in this field.

Suicidal behavior is the transformation of a self-harming thought, which is closely related to the concept of depression and impulsivity, into active action, which can be fatal. The psychological and socioeconomic aspects of suicidal behavior have been examined in many studies, but its neurobiological aspect has not been sufficiently elucidated.[2] Approximately 45.000 people in the United States[3] and more than 800.000 people worldwide die by suicide each year.[4] Diet plays a significant role in a person's mood and behavior. Amino acids are key precursors in the synthesis of neurotransmitters, hormones, and enzymes that play a role in the continuation of all vital functions in humans. There are 20 basic standard amino acids in nature, and these amino acids play a fundamental role in the control and regulation of both the physical and biological functions of the human body.[5,6] Amino acids, which are effective in all metabolic

processes in the body, are divided into two groups in terms of their biological importance: essential (exogenous) and non-essential (endogenous). Essential amino acids cannot be synthesized in the body; they must be taken from outside with food. Non-essential amino acids, which are necessary for the continuation of vital functions, are synthesized by the body. Essential amino acids; methionine, tryptophan, lysine, leucine, isoleucine, valine, threonine, phenylalanine and histidine. Methionine restriction is important in delaying the onset of neurodegenerative diseases and increasing body resistance to stress factors.[7] Tryptophan participates in the structure of serotonin and melatonin. Serotonin deficiency, known as the happiness hormone in humans, causes depressive and tired moods. The precursor amino acid serotonin, tryptophan, is also very important in this context. Lysine is one of the essential amino acids for the skeletal-muscular system and plays an important role in the production of muscle proteins, especially in sports injuries and post-surgery periods. Leucine acts as a stimulating signal in the body, especially during the developmental stage of babies, and accelerates the anabolic process, especially in muscle protein synthesis. It is also the most effective amino acid in delivering glutamate, an important excitatory neurotransmitter in the brain, to neurons. It significantly improves cerebellar symptoms.[8] Isoleucine; It plays a role in all physiological functions in the body such as growth, immunity, protein metabolism, fatty acid metabolism and glucose transport. Valine also plays an active role in cell metabolism (especially transamination, oxidative decarboxylation etc.).[9] Valine is oxidized in brain tissue and forms glutamine from glutamate. Thus, the brain protects itself against ammonia thanks to its amine group. Threonine is extremely important in protecting intestinal mucosal integrity, barrier function and also physiology.[10] Since histidine is used as a metabolite in histamine biosynthesis, when its deficiency occurs, anxiety, fatigue and depression symptoms are observed in humans since histamine release is reduced.[11] Leucine-histidine dipeptide reduces depression symptoms by suppressing primary microglia activation.[12]

METHODS

Each stage of the study was carried out in accordance with ethical rules. Prior to implementation, written permission was obtained from the Clinical Researches Ethics Committee of Sivas Cumhuriyet University (Date: 03.12.2019, Decision No: 2019-12/01). After the informed consent forms were read and informed to the patients and healthy volunteers or their legal heirs, a written consent form was signed. Afterwards, blood samples were taken from these volunteers and they were included in the study. The study is an article produced from a thesis and was completed in accordance with the Helsinki Declaration.

In the study, 35 people who applied to Sivas Cumhuriyet University Faculty of Medicine Emergency Medicine Department after a suicide attempt between July 2020 and December 2020 were evaluated as a patient group after detailed anamnesis and physical examination. Among the patients who applied to the emergency service between these dates, those who were suitable were included in the study. The control group was also selected from a population similar to the patient group in terms of age and gender. The study was based entirely on the principle of volunteerism within the scope of the informed consent form for both groups.

Patients with acute or chronic diseases (such as diabetes mellitus, hypertension, chronic renal failure, heart failure, liver pathologies), patients with autoimmune diseases, patients with infections, and those with eating habits different from normal were excluded from this study.

Approximately 10 ml of venous blood was taken from the patient and control groups and transferred to an EDTA and empty silicone tube. These blood samples were centrifuged at +4°C 4000 rpm for 5 minutes, and the plasma/serum obtained was portioned into 2 separate Eppendorf tubes. The blood samples were stored at -80°C until the relevant parameters were studied.

The plasma/serum samples obtained from the patient and healthy control groups were removed from the -80°C storage and thawed, and all amino acid levels in the plasma/serum were measured by the relevant laboratory with a Q-TOF LC/MS device. The data obtained from our study were loaded into the SPSS (ver:22.0) program and Kolmogorov-Simirnov, the significance test of the difference between two means, Man-Whitney U test, Chi-square test were used in the evaluation of the data and the error level was taken as 0.05. In this study, when $\alpha=0.05$; $\beta=0.10$ and $(1-\beta)=0.90$, it was decided to include 35 individuals in each group and the power of the test was found to be $p=0.90744$.

RESULTS

The mean age of the 35 patients evaluated in the study was 30.17±11.65 years and the mean age of the 35 individuals in the control group was 30.97±9.46 years ($p=0.15$; $p>0.05$).

22 (62.9%) of the individuals in the patient group were female and 13 (37.1%) were male; 22 (62.9%) of the individuals in the control group were female and 13 (37.1%) were male ($p=1$; $p>0.05$).

When the distribution of the groups according to educational status was evaluated; 17 (48.6%) of the individuals in the patient group were primary school and high school graduates and 18 (51.4%) were university and postgraduate graduates. 14 (40%) of the individuals in the control group were primary school and high school graduates; 21 (60%) are university and graduate graduates. The difference between the groups in terms of educational status is not statistically significant ($p=0.43$; $p>0.05$). While 14 (40%) of the patient group evaluated in the study had a psychiatric history, 21 (60%) did not have a psychiatric history. In the control group, 3 (5.7%) had a psychiatric history, and 32 (94.3%) did not have a psychiatric history. The current difference between the groups was found to be statistically significant ($p=0.01$; $p<0.05$) (**Table 1**).

When the suicide methods of the individuals in the group of 35 patients who applied to the emergency room after a suicide attempt were examined; 32 of the patients (91.4%) applied after taking medication, 1 (2.9%) jumped from a height, and 2 (5.7%) self-harmed with a sharp object.

When the types of medications taken by the individuals in the patient group who committed suicide by taking medication were evaluated; 11 (31.4%) of the patients committed suicide by antidepressants, 7 (20%) by analgesics and antibiotics,

Table 1. Comparison of groups in terms of gender, age, education status and psychiatric history

	Patient group n (%)	Control group n (%)	Ki kare test
Gender			p=1
Female	22 (62.9)	13 (37.1)	
Male	22 (62.9)	13 (37.1)	
Average age	30.17	30.97	p=0.15
Education status			p=0.43
Primary school+high school	17 (48.6)	14 (40)	
University+postgraduate	18 (51.4)	21 (60)	
Psychiatric history			p=0.00*
Yes	14 (40)	3 (5.7)	
None	21 (60)	32 (94.3)	

* p<0.05

6 (17.1%) by nonsteroidal anti-inflammatory drugs, and 3 (8.6%) by antiepileptic drugs.

When the essential amino acids were examined in general, the amino acids methionine, leucine, isoleucine, valine, lysine, threonine, phenylalanine and tryptophan were found to be significantly lower in the patient group in the comparison made between the patient and control groups (p<0.05). However, no statistically significant difference was found in the comparison between the two groups for histidine amino acid (p=0.405; p>0.05) (**Table 2**).

Table 2. Comparison of essential amino acids between groups

Aminoacids	Patient mean±SD	Control mean±SD	t test (p value)
Methionine	25±6	30.9±6.6	<0.001*
Leucine	101.6±25.8	125.2±23.3	<0.001*
Isoleucine	73.4±18.7	92.8±20.3	<0.001*
Valine	171.6±41.9	205.8±38.04	0.001*
Lysine	150.4±29.5	169.4±31.6	0.011*
Threonine	115.9±37.3	140.8±34.4	0.005*
Phenylalanine	50.4±13.6	58.9±32.5	0.008*
Histidine	75.7±7.09	77.4±9.33	0.405
Tryptophan	45.1±10.4	59.2±9.7	<0.001*

*p<0.05, SD: Standard deviation

DISCUSSION

When we examine the data obtained in the study; as in many studies examining the suicidal behavior of the patient population applying to the emergency room after a suicide attempt, it was found to be higher in women (female:male ratio 1.69:1). Women have higher rates of suicidal ideation and behavior than men.[13-16]

When the sociodemographic and socioeconomic characteristics of the patients are considered; the results are similar to different studies.[17,18] Suicidal behavior was found to be higher in people with low social status. In another study examining the effect of socioeconomic levels on suicidal behavior, unemployment stood out as a situation that increases the risk of suicide. The probability of suicide attempt increases as the duration of unemployment increases.[19]

Psychiatric history was detected in 40% of the patients applying after a suicide attempt. There are different clinical studies showing a significant link between suicidal behavior and psychiatric disorders, and in this context, our study overlaps with many clinical studies.[20,21] Psychiatric disorders in particular have been accepted as an important risk factor for suicide attempts.[15,22]

When the suicide methods in our study were evaluated, it was seen that 91.4% of the patients applied with drug intoxication. When the drugs taken by the patients applied with drug intoxication were evaluated, they most frequently preferred antidepressants that they used for treatment purposes. This was followed by self-harm with a sharp object at 5.7% and jumping from a height at 2.9%. The rates determined regarding the suicide method were not subject to discrimination for women and men in our study. When different studies were evaluated, it was determined that men usually died by suicide by hanging, carbon monoxide poisoning, and gunshot wounds; while it was emphasized that women mostly exhibited suicidal behavior by taking drugs.[13,15,16,23]

In our study, all essential amino acids (leucine, isoleucine, valine, methionine, threonine, lysine, phenylalanine, and tryptophan), except for histidine, were found to be significantly lower in the patient group compared to the control group (**Table 2**). As it is known, essential amino acids are essential amino acids that must be taken externally. Low levels of these amino acids in the patient group showed that nutrition and protein intake were significantly reduced in patients with depressive mood. Essential amino acids (leucine, isoleucine, valine) that regulate the skeletal-muscular system and energy metabolism were significantly lower in the patient group (p=0.001; p<0.05).When the amino acids that are examined in relation to depression and important clinical studies in the literature are considered, methionine facilitates the synthesis of important neurotransmitters such as serotonin, norepinephrine, and dopamine, which affect the mood in the body and give people a sense of happiness and vitality.[24-26] Therefore, the low levels of methionine in the suicidal patient group with depressed mood in our study was an important result (p<0.001; p<0.05). Since phenylalanine, one of the essential amino acids, plays a role in the synthesis of norepinephrine, some forms are used in the treatment of depression. In its deficiency; anorexia, loss of appetite, weakness, and depression can be seen.[27] Depressive and tired moods are also seen in the deficiency of tryptophan, which is included in the structure of serotonin and melatonin.[28] Almost all physical and psychological stress factors affect serotonin levels in the human body. Tryptophan amino acid, which directly affects serotonin levels, was also found to be significantly low in the patient group in our study (p<0.001; p<0.05).

In our study, we determined the relationship between suicidal behavior and essential amino acid amount analyses in plasma by considering the sociodemographic characteristics of the patients. We evaluated the precursor amino acids responsible for every stage of both physiological and psychological processes in humans.

The frequency of suicidal behavior has started to increase in recent years. Since emergency services are the first places

to apply after suicide attempts, evaluations and statistical analyses conducted in emergency services in particular should have clinical importance in the literature.

CONCLUSION

There are many studies examining the relationship between factors such as diet, socioeconomic level, psychiatric history, demographic characteristics, etc. and suicide attempts. There are also studies examining the relationship between suicidal behavior and depression and certain amino acids taken due to nutrition. However, our study is the only comprehensive study based on measuring essential amino acid levels in the body along with socioeconomic and demographic characteristics, as it was conducted in the emergency department during the acute period. Despite this, being a single-center study has a restrictive effect on generalizability. Based on our study results, we believe that suicide attempts can be prevented by increasing neurobiological and mental activity along with regular protein intake, nutrition, and exercise. We also believe that studies with high participation will yield results that support our study.

ETHICAL DECLARATIONS

Ethics Committee Approval

Prior to implementation, written permission was obtained from the Clinical Researches Ethics Committee of Sivas Cumhuriyet University (Date: 03.12.2019, Decision No: 2019-12/01).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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