

Comorbidity of Mental and Somatic Pathology in the Study of the Association of Blood Folate Levels

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Abstract

This research work focuses on comorbidity, which links a complex of somatic and mental pathologies in patients with diagnosed bipolar personality disorder and the development of cardiovascular catastrophe in the form of ischemic stroke. The authors consider it promising and relevant to study the role of deficiencies of certain nutrients and the influence of this factor on the appearance and development of various mental disorders, in particular, the level of folate in the blood serum to prevent the development of cardiovascular catastrophe in patients with bipolar personality disorder. The core of the randomized study included 18 patients with diagnosed bipolar disorder and 20 healthy people with a history of ischemic stroke by mental status. The practical results of the work confirm the current literature data on a decrease in the concentration of folates in the blood of patients with bipolar disorder and diagnosed ischemic stroke, which proves the relationship between the mental and somatic components and impaired metabolism of folic acid derivatives. The information obtained should serve as a trigger for the search for an evidence-based strategy for managing this cohort of patients in the key point prevention and correction of the existing disease.

Keywords: Somatic pathology, Manic personality disorder, Comorbidity, Folic acid, Ischemic stroke, Homocysteine

INTRODUCTION

Currently, the term "comorbidity" is the consolidation of several diseases in the body associated with common pathomechanisms and having common direct and indirect etiological factors [1, 2]. To date, a whole layer of research direction has been formed in medicine, which studies the comorbidity of mental and somatic diseases [3, 4]. The formation of this layer has actively begun only in recent decades with the development of modern science as a whole [5, 6]. However, since the time of the Renaissance thinkers, there have been postulates according to which the essence of man at all times excluded the duality of the psyche and soma [7, 8]. Currently, such sciences as psychoneuroendocrinology, anthropology, psychoneuroimmunology, and even genetics are studying the neurobiological foundations of human somatopsychic integrity. The genome study, for example, against the background of various results of parthenogenesis, which include common somatic and mental disorders, indicated that most of them are characterized by a high degree of polygenicity [9, 10]. This information is a breakthrough because it confirms the participation of a large number of genes associated with the risk of developing somatic diseases in the mental background. This became clear after a clear tracing of the links between the development of cancer, cardiovascular diseases, diabetes mellitus, polycystic ovaries

in women, and other pathologies with mental disorders [11-15].

The new data give scientists reasonable hope for the possibility of patronage and reducing the risks of having children with similar associations in the future. This will happen due to the editing of genomic architectures, elimination of nutrient deficiencies in people at increased risk (the authors assume that the risk group includes patients with a burdened hereditary history of psychiatric profile), as well as the elimination of endocrine diseases [16, 17].

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Bipolar affective disorder (BAD) is a common chronic recurrent pathology of the psychogenic spectrum, having an endogenous etiology. BAD most often manifests itself in the form of several affective disorders of varying intensity and severity. It includes manic, hypomanic, and depressive phases, which may alternate throughout life or exist as an intermission throughout the patient's life [18]. The duration of the phases ranges from one and a half to two years, and manic phases, as a rule, are several times shorter than depressive ones. As practice shows, the danger and greater level of damage in patients with BAD is observed precisely in the phases of bipolar depression because patients spend more time in depression, increasing the risk of suicide [19].

The etiology and pathogenesis of bipolar disorder are not completely clear. The results of modern neuroendocrine and genetic studies in different countries in this direction make it possible to assume that the disease has a complex pyramidal etiology and pathogenesis. The importance of several biological factors interacting with environmental influences and various psychosocial interactions plays a role here. The disease usually manifests at a young age and is much more common in women [20]. As a rule, the management of patients with BAD includes lifelong pharmacotherapy to relieve symptoms and achieve remission, as well as prevention of relapses [21, 22].

The role of metabolic disorders of folic acid derivatives, particularly folates, in the etiopathogenesis of some mental diseases, has been accelerated over the past few decades in the scientific literature [23]. Due to the appearance of more and more scientific papers on the role of nutrient deficiencies, in particular, folate in the blood serum of mentally ill patients [24, 25], in particular, BAD [26-28], researchers became interested in this topic in the key of a predictor of the development of cardiovascular catastrophes in this group of patients. It is known that with insufficient folic acid and folate in the body, there is a possibility of developing hyperhomocysteinemia [29].

Hyperhomocysteinemia is a risk factor for the development of cardiovascular disasters. The risk of ischemic stroke in this situation is due to excessive accumulation of homocysteine in the body: loosening of the vessel walls and the formation of local defects in the endothelium occurs. This can cause cholesterol and calcium to settle in the vascular wall [29].

Folates are water-soluble compounds based on folic, or pteroylmonoglutamic, acid. In turn, folic acid, being a coenzyme of several enzymes, transfers single—carbon fragments during the biosynthesis of many other compounds in the body: a methyl group during the biosynthesis of methionine and thymine, an oxymethyl group during the biosynthesis of serine, a formyl group during the neoplasm of purine bases. Folic acid and its derivatives are consumed by cells in the form of its active metabolites, for example, 5-methyltetrahydrofolate, which is needed for transport and assimilation in various tissues, especially rapidly dividing.

Folic acid is necessary to participate in the processes of DNA replication. Violation of these processes leads to an increase in the risks of cancer and megaloblastic anemia, etc. [30]. The reference values of the folate level in the blood vary in different literature sources and schools. However, in Russian clinical guidelines, the range from 7 to 22 mg in serum is considered the norm.

The reduction of folate and folic acid reserves in the body occurs relatively quickly when certain causes appear. This condition has been noticeable for two weeks thanks to a dynamic blood test. The most common cause, as a rule, is alimentary insufficiency, intestinal malabsorption, hemodialysis, or the use of medications: antiepileptics, barbiturates and their derivatives, immunomodulators, metformin, semaglutide, etc. [31-33].

MATERIALS AND METHODS

A randomized study was conducted based on the diagnostic polyclinic center in Grozny (Chechen Republic, Russia). It involved 18 patients of both sexes with diagnosed bipolar disorder (n1=18), as well as 20 patients of both sexes who were healthy in mental status but had a history of ischemic stroke (n2=20). The examination of patients and healthy people was carried out from March 2012 to August 2023.

Table 1 lists the main criteria for selecting patients.

Table 1. Patient selection criteria

Inclusion criteria	Exclusion criteria
<p>Group 1 (n1=18)</p> <ul style="list-style-type: none"> - age from 18 to 75 years; - a history of bipolar disorder; - informed consent to participate in the study; - no use of chemotherapy, radiation, or high-dose steroid therapy for 1 month before inclusion in the study. <p>Group 2 (n2=20)</p> <ul style="list-style-type: none"> - absence of previously registered mental disorders throughout life; - age from 18 to 75 years; - a history of one or more episodes of ischemic stroke - informed consent to participate in the study. 	<ul style="list-style-type: none"> - decompensated somatic pathologies; - dependence on dialysis; - pregnancy; - leukemia; - lymphoma; - HIV/AIDS.

Research material: venous blood serum. The material was taken on an empty stomach in the morning with the help of vacutainers. Determination of folate concentration was carried out by chemiluminescent immunoassay on microparticles.

Statistical processing of the results of the study was carried out using the application software package "Statistica 10.0" ("StatSoftInc," USA) and the statistical program for Windows "Primer of Biostatistics 4.03 by Stanton A. Glantz, 1998 McGraw-Hill".

RESULTS AND DISCUSSION

The duration of the disease from the moment of manifestation was eleven months and ten days. **Table 2** shows the average values of folate content in blood serum.

Table 2. Characteristics of respondents by the level of folate concentration in the blood in the study and control groups

Indicator	Group 1 (n=18)	Group 2 (n=20)
Gender: Female/Male	10/8	10/10
Age, years (average value)	28	32
Serum folate level (average value)		
All patients	3,310	4,50
Female	3,20	4,75
Male	3,40	3,70

All respondents received group 1 therapy for bipolar disorder: 4 in the hospital and 14 on an outpatient basis. Differences in folate levels between sick and healthy people were more pronounced in females and statistically insignificant in males with the available number of observations (**Table 1**). When comparing the results obtained with the reference values, it can be noted that in all the studied groups (including group 2 patients), the vast majority of the examined patients have folate levels below the median (9.95 ng/ml): Folate levels below the reference values were observed in 14 (77.7%) patients. There was no association of folate levels in the blood with the age of the study participants. However, the purity of detection of ischemic stroke increased with age in the participants.

CONCLUSION

The data of our study confirm the need to build a scientific and evidence-based strategy for managing patients with folic acid deficiency in the key point prevention and correction of cardiovascular risks not only in ordinary patients but also in patients of the psychosomatic spectrum. There is practical evidence of a correlation between folic acid derivative deficiency, cardiovascular risk, and cognitive disorders. The management of patients with bipolar affective disorder should include not only standard diagnostic procedures but also neurohormonal and biochemical methods in dynamics from the moment of manifestation of the disease.

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