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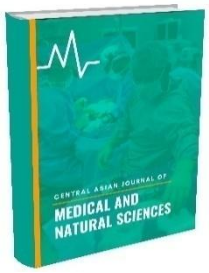

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Cognitive Impairments in Patients with HIV - Associated Encephalopathy

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Abstract: HIV infection is one of the most pressing medical and social problems worldwide today. This article discusses one of the types of complication of HIV-infection as HIV-associated encephalopathy. The clinical features and diagnostic criteria of the disease are considered. Patients were examined using the Montreal Cognitive Assessment Scale and symptomatic treatment with the nootropic drug choline alfoscerate was carried out.

Key words: HIV infection, human immunodeficiency virus, acquired immunodeficiency syndrome, cognitive status, encephalopathy, MoCA test, choline alfoscerate.

Introduction

The possibility of treating HIV-infected patients with the use of antiretroviral drugs has reduced the death rate from AIDS by several times. In this regard, new challenges are being put forward for healthcare to improve the quality of life of HIV-infected people. An important task that requires special attention is the correction of disorders of the central nervous system in HIV-infected patients. The use of antiviral therapy has increased the life expectancy of patients with HIV infection, however, to date, such drugs that could completely eradicate the virus from the body. In this regard, it is necessary to deal with the pathological effect of the virus on body tissues, including nervous tissue, throughout the life of an HIV-infected patient.This task is not only a medical, but also a social problem, since HIV is characterized by the defeat of young and working age, and lesions of the nervous system are often detected already in the early stages of the disease. Impairment of cognitive processes creates certain difficulties in study, work, daily activities and personal life of patients with HIV. About 1/3 of HIV-infected people are in the age range of 15-25 years. On average, this is about 3,000 new infections per day. [1]

The CNS has two unique barriers that protect it from the effects of chemical and biological pathological factors. The cells of the blood-brain barrier are "sewn" together by tight bonds through which many cells cannot pass. From the side of the brain, the barrier is covered with a thin basement membrane. Pericytes are located on the membrane from the side of the nervous tissue. They are located along the capillaries and have a long process structure. The processes braid capillaries and form tight bonds with endotheliocytes . There is evidence that pericytes can move, taking over the

functions of macrophages. These cells are thought to be able to replicate and differentiate into osteoblasts, adipocytes , chondrocytes , smooth muscle cells, and others. The version that these cells may have the ability to differentiate into cells of the nervous tissue is not ruled out, which is currently being actively studied. In recent studies, data have been obtained indicating that a decrease in the number of pericytes in the CNS leads to impaired BBB permeability, and pathologies of neurocognitive processes associated with these disorders. The processes of astrocytes also have indirect protection functions , which tightly braid the vascular wall in the nervous tissue, creating a case for the capillaries of the brain. [2]

The hematoliquor barrier is built from the cuboidal epithelium of the choroid sinus. It is also characterized by a close interweaving of cells with the formation of tight junctions, which prevents the transport of many pathogenic substances to the brain and spinal cord. However, this barrier is much weaker than the BBB, since the main function of this barrier is to maintain the required amount of cerebrospinal fluid. The most popular theory is the penetration of the virus through the BBB with infected cells. Lymphocytes and monocytes become infected with the virus immediately before entering the CNS. After infection, they penetrate the BBB, where monocytes transform into perivascular macrophages, which have the ability to transmit the virus to other cells of the nervous tissue. [3]

According to many scientific data, the endothelium of the vascular wall does not have CD4 receptors and co-receptors CCR5 and CXCR4. Most of the scientific evidence available to date indicates that there are no CD4 receptors in the cells of the walls of cerebral vessels, or they are present in a very small amount. At the same time, there are C-type lectins (MBL , mannose -binding lectin) on the surface of nerve cells , which have similar functions to the DC-SIGN of dendritic cells. Their only difference is that their affinity for gp120 of the virus is weaker. An important feature of the virus is its ability to enhance the expression of DC-SIGN, which contributes to the fact that the virus actively moves and multiplies in the nervous tissue. [4]

An interesting fact is that in the urogenital tract, due to the absence of CD4 receptors in its epithelium, the virus uses the same mechanism for penetration and reproduction. The gp120 virus protein reacts with the C-type lectin of the epithelial wall. The result of this process is the destruction of tight intercellular junctions, due to which the virus gains access to CD4 receptors located in the mucous membrane. The dense epithelial barrier is only permeable to particles up to 30 nm in size , and the virus is known to be 80-100 nm in diameter. However, HIV passes through this barrier in 120 minutes. [5]

The penetration of the virus into the CNS can also occur through the intercellular gaps of the endothelial wall. This mechanism is quite possible in the later stages of HIV infection, when under the action of toxins and other pathogenic agents the endothelial wall is destroyed, intercellular contacts are weakened and become easily accessible for the penetration of infectious particles. The virus can easily diffuse through such weakened contacts. The subsequent destruction of the nervous tissue occurs as a result of the direct effect of the virus on the brain cells. The addition of secondary diseases further worsens the state of the BBB, causing local inflammatory processes. [6]

In the absence of adequate antiretroviral therapy, encephalopathy develops in 2/3 of HIV-infected patients. Signs of encephalopathy are detected in 25% of cases even at the stage of the absence of clinical manifestations of AIDS, and in 3-5% of cases they are the first manifestations of disease progression [7]. HIV encephalopathy is a special clinical syndrome of subcortical-frontal dementia that develops under the direct influence of the virus on the tissues of the nervous system and is characterized by motor, cognitive and behavioral disorders [6]. The question of at what stage of HIV infection neurological disorders begin to develop is still open.

Damage to the nervous tissue occurs as a result of direct (with the participation of viral proteins) and indirect (inflammation) mechanisms [7]. Each model of damage implies infection of macrophages and microglia with viral particles at the initial stage . The direct mechanism of damage implies the death of neurons under the direct influence of viral proteins [8]. The second model explains neuronal damage through the inflammatory process of brain tissue in response to HIV integration. Both of these mechanisms can be present simultaneously at any stage of HIV infection [9]. The virus is not detected in the neurons themselves, however, various immunopathological mechanisms triggered by the presence of HIV in the nervous tissue cause functional and structural changes in neurons [10].

Virus-infected brain cells produce viral particles and inflammatory mediators. Due to their cytotoxic properties, densely packed endotheliocytes are destroyed , which leads to a decrease in the total number of neurons and destruction of the myelin sheath of cells [11]. Viral replication also affects the functioning of oligodendrocytes and astrocytes . The neurotoxic effect of the viral protein gp120 has a detrimental effect on neurons, the effect of which is also due to the effect on neurotransmitter processes, which ultimately leads to the inevitable death of neurons [10,11].

The purpose of the study . The study of the cognitive status of HIV-infected patients, the study of the effect of nootropics on the cognitive status of patients with HIV-encephalopathy.

Materials and Methods: For the study, 23 patients were randomly selected who were treated at the Fergana branch of the Republican AIDS Center. Among them, 13 men (56.5%) and 10 women (43.5%), the average age of patients is 31.7 ± 1.1 years. For the study of cognitive function, a battery of tests was chosen - the Montreal Cognitive Function Assessment Scale or abbreviated MOCA - a test as the most sensitive and convenient for the study of patients with cognitive impairment. The collection of one-line tests consists of 30 items and is completed in an average of 12 minutes. [8] This scale assesses the seven most significant cognitive functions, which include: short-term memory (5 points), spatial -visual ability (4 points), aspects of executive function (3 points), attention and concentration (5 points), language functions (5 points), abstract thinking (2 points), orientation in time and space (6 points). The maximum score for this test is 30, of which 26 to 30 is normal, 22 to 25 means mild cognitive impairment, 17 to 21 moderate cognitive impairment, and 16 or below severe cognitive impairment. [8,9] To correct cognitive impairment in patients with HIV-encephalopathy, we decided to use choline alfoscerate at a dosage of 1000 mg intravenously for 10 days and then continue treatment with choline alfoscerate in tablet form 400 mg for 6 months.

Research results. As a result of the study, it was found that the average score of the MoCA test among patients is 21.6 ± 0.85 points. Data on the severity of cognitive status disorders are displayed in Table No. 1 from which it follows that the main contingent of patients falls at the level of mild cognitive disorders

Table #1

Degree of cognitive deficit	Frequency of occurrence
No cognitive impairment	3 (13%)
With light CI	15.(65%)
With moderate CI	4(17.4%)
With heavy CI	1 (4.3%)

Patients were divided into groups depending on the duration of morbidity. The average indicators of the degree of cognitive impairment depending on the duration of the disease are shown in Table No. 2

Table number 2

Duration of HIV	MoCA test result
1 to 3 years	22.4±1.25
4-6 years old	22.1±0.84
7-10 years old	20.6±1.21
10 years or more	22.5±1.32

The patient, regardless of the antiretroviral drug taken, was prescribed the drug choline alfoscerate at a dosage of 1000 mg intravenously for 10 days, after which they continued treatment with the tablet form of the drug choline alfoscerate at a dosage of 400 mg for 6 months. Several repeated studies of cognitive status were conducted, the results of which are displayed in Table No. 3

Table No. 3

	Before treatment	After 10 days	After 1 month	In 3 months	In 6 months
MoCA test result	21.6±0.8	22.8±0.84	22.9±0.82	23.1±0.8	23.8±0.71

When using the injectable form of the drug for ten days, there was a slight improvement, after which the rate of improvement slowed down during the first three months of treatment. Based on the results, it can be determined that only after a long-term treatment of at least 6 months can a statistically significant improvement in the patient's cognitive status be obtained ($p< 0.05$).

Table No. 4

cognitive functions	Frequency of cognitive impairment before treatment	Frequency of cognitive impairment after treatment
1) orientation in time	14.6±4.2	13.2±6.1
2) orientation in place	7.4±3.1	7.1±3.9
3) self-orientation	0	0
4) involuntary memory	87.4±4.5	74.5±5.8
5) understanding of speech and complex logical and grammatical structures	28.0±6.5	26.5±7.8
6) expressive speech	16.8±4.2	15.0±5.8
7) dynamic praxis	46.2± 6.8	35.4± 7.6
8) constructive praxis	53.6±6.3	38.3±8.6
9) reading	28.2±6.5	24.5±7.0
10) letter	35.3±6.8	30.7±7.4
11) focus	80.3±5.3	64.6±9.3

When deploying cognitive status during treatment, it can be seen that the main improvements affected involuntary memory, concentration, dynamic and constructive praxis to a greater extent than speech, reading and writing. There was practically no improvement in such cognitive functions as orientation in time, place and self.

Conclusion:

1. The study of the cognitive status of patients with HIV encephalopathy shows the predominance of a mild degree of cognitive impairment, in contrast to earlier studies, which may be associated with the use of highly active antiretroviral therapy.

2. The duration of the course of HIV directly affects the state of cognitive status, the worst result of which shows the duration of the disease from 7 to 10 years.
3. The results of a dynamic neuropsychological examination using the drug choline alfoscerate revealed significantly positive dynamics in the form of an increase in the level of cognitive status by an average of 2.2 points on the Montreal Cognitive Function Assessment Scale .

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