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Nootropic Drugs and Cognitive Disorders in HIV Encephalopathy

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Abstract After the immune system, the most common complication of HIV infection is neurological complications. HIV encephalopathy is the most common form of neurological complications of HIV infection. In this publication, we decided to test the correlation of the viral load of patients with the severity of the disease, as well as the effectiveness of some nootropic drugs, such as choline alfoscerate and hopantenic acid. 100 patients with HIV encephalopathy for the experimental group and 25 patients with HIV infection but without signs of NeuroAIDS for the control group were randomly selected for the study. As a result patients underwent neuropsychological and cognitive studies before and after the use of nootropics. The benefits of this study showed the independence of the viral load and the level of CD4 lymphocytes from the severity of HIV - encephalopathy. With a profound impairment of cognitive impairment, the drug choline alfoscerate showed a higher result, with a high degree of anxiety, a drug with hopantenic acid showed a better result. Laboratory indicators of HIV infection cannot diagnose the severity of HIV encephalopathy. The choice of nootropic drug depends on the results of cognitive and psycho-emotional tests.

Keywords HIV – encephalopathy, Viral load, Cognitive disorders, Choline alfoscerate, Hopantenic acid

1. Introduction

After the immune system, the most common complication of HIV infection is neurological complications. HIV encephalopathy is the most common form of neurological complications of HIV infection. In this publication, we decided to check the correlation between the viral load of patients and the severity of the disease, as well as the effectiveness of some nootropic drugs, such as choline alfoscerate and hopantenic acid.

Research methods. For the study, 100 patients with HIV encephalopathy were randomly selected for the experimental group and 25 patients with HIV infection but without signs of NeuroAIDS for the control group. The patients underwent neuropsychological and cognitive studies before and after the use of nootropic drugs.

Results: The results of the study showed the independence of the viral load and the level of CD4 lymphocytes from the severity of HIV encephalopathy. In case of profound impairment of cognitive impairment, the drug choline alfoscerate showed a better result; in case of a high degree of anxiety, the drug with hopantenic acid showed a better result.

Conclusions: Laboratory indicators of HIV infection cannot diagnose the severity of HIV encephalopathy. The choice of nootropic drug depends on the results of cognitive and psycho-emotional tests.

The human immunodeficiency virus is characterized by increasing suppression of the immune system and the development of acquired human immunodeficiency syndrome, characterized by inevitable progression with a fatal outcome for humans. HIV and AIDS are two different concepts, since the presence of HIV infection does not mean the presence of AIDS. The virus can persist throughout the body for a long time without showing any clinical signs of infection [20].

The first fatal manifestations of complications associated with HIV infection, manifested in the form of Pneumocystis pneumonia and Kaposi's sarcoma, were noted in 1981 in Los Angeles and New York [21]. Since 1983, HIV has been detected in women who became infected through sexual contact from partners. In Russia, the first cases of HIV infection were identified in the early 1980s. Immunodeficiency virus has become a serious health problem worldwide, being one of the most complex and severe infectious diseases [22].

WHO identifies 3 major and 6 minor symptoms of AIDS. Major symptoms of AIDS include weight loss of 10% or more, diarrhea lasting more than a month, and fever lasting more than a month. Minor symptoms of AIDS include a persistent cough for a month, generalized pruritic dermatitis, oropharyngeal candidiasis, recurrent herpes zoster, chronic herpes simplex virus infection, and generalized encephalopathy.

In accordance with this division of symptoms, the diagnosis of AIDS is made when at least two major and at

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least one minor symptoms are detected in an infected person. It is also worth noting that the detection of generalized Kaposi's sarcoma or cryptogenic meningitis in a patient is already a diagnostic criterion for AIDS.

The virus easily penetrates the blood-brain barrier, thereby entering the tissues of the central and peripheral nervous system [16]. Lesions of the central nervous system, which are the second most common lesion in HIV after the immune system, are detected at any stage of the disease: 20% of HIV-infected people develop lesions of the nervous system at the stage of absence of clinical manifestations of the disease. In the stage of a developed clinical picture of the disease, central nervous system lesions occur in 40-50% of patients. In the later stages of AIDS, more than 90% of patients have varying degrees of damage to the central and peripheral nervous system [17].

Many studies have been devoted to studying the characteristics of the impact of HIV on the central nervous system. The virus is neurotropic and is characterized by early damage to the nervous system. However, the features of virus penetration into the central nervous system remain insufficiently studied.

To date, four possible routes for the virus to enter the brain in the early stages of human infection are being considered:

1. penetration of HIV through the choroid plexuses located at the base of the brain; the carrier of the virus is the blood;
2. penetration into the nervous system through infected macrophages and lymphocytes through the blood-brain barrier;
3. transport through cranial nerves;
4. receptor and non-receptor transport across the blood-brain barrier.

The functions of the blood-brain barrier are to protect the brain from the penetration of damaging factors, as well as toxic substances that can cause any harm to the central nervous system. The BBB consists of the endothelium of brain vessels, the basement membrane, which contains cellular and fibrillar components, and the perivascular glia and astrocytes. The role of astrocytes is that with their processes they create a powerful framework around the endothelial wall, covering 95% of their area.

The possibility of treating HIV-infected patients with the use of antiretroviral drugs has reduced the mortality rate from AIDS several times. In this regard, healthcare is facing new challenges to improve the quality of life of HIV-infected people. An important task that requires special attention is the correction of central nervous system disorders in HIV-infected patients. The use of antiviral therapy has made it possible to increase the life expectancy of patients with HIV infection, however, today there are no drugs that could completely eradicate the virus from the body. In this regard, it is necessary to combat the pathological influence 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 typically affects young people of working age, and damage to the nervous system is often detected in the early stages of the disease. Impaired cognitive processes create 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 approximately 3,000 new infections per day.

The central nervous system has two unique barriers that protect it from the effects of chemical and biological pathological factors. The cells of the blood-brain barrier are “stitched” together by tight bonds through which many cells cannot pass. On the brain side, the barrier is covered with a thin basement membrane. Pericytes are located on the membrane on the nervous tissue side. They are located along the capillaries and have a long process structure. The processes entwine capillaries and form tight connections with endothelial cells.

The purpose of this study was to study the degree of cognitive and emotional impairment in patients with HIV encephalopathy. Conduct laboratory tests (PCR load, complete blood count) in patients with HIV encephalopathy. To study the effect of nootropic drugs (hopantenic acid and choline alfoscerate) on cognitive, emotional and focal neurological disorders in patients with HIV encephalopathy.

2. Materials and Methods of Research

The study is conducted with the participation of 100 patients with HIV encephalopathy. The age of the studied patients was from 25 to 60 years. The control group will include 25 HIV-infected patients without neurological complications.

During the study, cognitive and emotional status was assessed through neuropsychological tests (MOCA test, FAB test, Spielberg-Hanina test), clinical and instrumental analysis (electroencephalogram and magnetic resonance imaging).

3. Result and Discussion

From the life history of the patients in the main group, it was established that all patients with HIV encephalopathy in childhood grew and developed without pathologies. During childhood, all study participants had only childhood infections. From the medical history, it was established that almost all patients with HIV encephalopathy have been HIV-infected for several years. In 76 (76%) patients, HIV infection was diagnosed more than 20 years ago, in 18 (18%) patients, HIV infection was diagnosed 18-20 years ago. 4 (4%) patients were unable to clarify the duration of infection and diagnosis of this infection. The largest number of patients with HIV encephalopathy have a long period of HIV infection.

The diagnosis of HIV infection was established only when clinical symptoms of the disease appeared in 74 (74%) patients with HIV encephalopathy. In the remaining 26 (26%) patients, HIV infection was diagnosed as an incidental finding during examination for other diseases.

An analysis of possible routes of transmission showed that 79 (79%) patients were infected through sexual contact, 18 (18%) patients noted the parenteral route of infection, and 3 (3%) patients could not specify the route of infection. Thus, the predominant route of infection among study participants was sexual transmission.

All study participants had their viral load and CD4 cell count determined. Statistically processed data are presented in Table 1.

As can be seen from the table, most patients have a low viral load. Only 7 (7%) patients had an average VL level, the mean value was 34,697.14 copies. The average VL in the category of patients with a high viral load of 100,000 or more copies was 1,967,577.91 copies. The average total viral load was 21,686.99 copies. The smallest VL was 36 copies, the largest was 9,402,553 copies.

The level of CD4 cells in study participants was also determined. Statistically processed results are presented in Table 2.

The vast majority of study participants had a fairly high level of CD4 cells along with a low VL, which indicates the effectiveness of ART. 79 (79%) patients had stage 4A HIV infection, and 21 (21%) patients had stage 4B HIV infection. The average age of patients with stage 4A was 34.6 ± 1.9 years. The average duration of the disease was 41.9 ± 16.5 months. The average age of patients with stage 4B disease was 39.7 ± 1.3 years, the average duration of the disease was 43.2 ± 1.4 months.

The third control group included 25 patients without signs of HIV encephalopathy. This group included 16 men (mean age 37.4 ± 1.2 years) and 9 women (mean age 39.9 ± 1.4 years); the mean age of the patients was 38.8 ± 1.3 years. Participants in the control group were assessed for VL and the level of CD4 cells in the blood to clarify the stage of the disease and the state of the immune system (Table 3).

The average viral load in the control group was 21,686.99 copies. The level of viral load up to 10,000 copies in the control group was in 12 (48%) patients. In 4 (16%) patients, VL was in the range of 10,000 – 100,000 copies, with an average of 43,967.36 copies. In 5 patients, VL was in the range of 100,000 or more copies and its average value was 371,754.17 copies (Table 4).

With a CD4 cell value of 200-350/ μl, the control group included 7 (28%) patients; the average CD4 level was 142.18/ μl. With a CD4 level of 350 or more, the control group included 18 (72%) patients with an average CD4 level of 471.54/ μl. The average CD4 level of 25 patients in the control group was 493.48/ μl. Based on the CD4 level, 7 (28%) patients in the control group were diagnosed with stage 4B of HIV infection, and 18 (72%) patients were diagnosed with stage 4A of HIV infection.

Table 1. VL level of study participants

VL level (copies)	Number of patients	Average value of VL	Min	Max
Up to 10,000	82	386.17	36	7 340
10,000-100,000	7	34,697.14	10 372	78 603
100,000 or more	11	1,967,577.91	118 168	9 402 553
Total	100	21,686.99	36	9 402 553

Table 2. Level of CD4 cells in the blood of patients with HIV encephalopathy

CD4 level	Number of patients	Average CD4 cell count	Min	Max
200-350	21	136.54	102	198
350 or more	79	486.19	201	1204
Total	100	493.48	102	1204

Table 3. VL in the blood of participants in the control group

VL level (copies)	Number of patients	Average value of VL	Min	Max
Up to 10,000	12	376.13	42	6,840
10,000-100,000	4	43,967.36	11 310	87 360
100,000 or more	5	371,754.17	116 178	6 313 493
Total	25	21,686.99	42	6 313 493

Table 4. Level of CD4 cells in the blood of participants in the control group

CD4 level	Number of patients	Average CD4 cell count	Min	Max
200-350	7	142.18	104	179
350 or more	18	471.54	214	1 170
Total	25	493.48	104	1 170

During the initial examination, patients with HIV encephalopathy complained of decreased mental functions (99%), poor sleep (95%), decreased mood (95%), headaches (73%), impaired coordination of movements (88%), and decreased performance (100%). Objective examination revealed convergence disorder (28%), signs of oral automatism (74%), pyramidal insufficiency (67%), coordination disorders (89%), amyostatic syndrome (43%).

It was also found that when tested according to the Spielberg-Hanina system, situational anxiety in patients in the control group without signs of HIV encephalopathy had a low level of anxiety (p = 0.01). Personal anxiety of patients in the control group also had a low level (p = 0.03). The frontal dysfunction battery test showed that in patients in the control group without signs of HIV encephalopathy, the study indicators were within the reference values. Testing on the MoCA scale also did not reveal any abnormalities in patients in the control group without signs of HIV encephalopathy (Table 5).

In the group of patients receiving hopantenic acid, complaints of mood swings and poor sleep decreased significantly. If before the start of treatment 47 patients complained of poor sleep, after treatment only 17 patients, the remaining patients noted normalization of sleep. Mood swings were a concern before the start of treatment in 46 patients of this group; after treatment, only 18 patients noted such a complaint.

Indicators of neurocognitive functions of patients of the first subgroup before and after treatment are presented in Table 6.

After a course of therapy with hopantenic acid, patients in the first subgroup moderately improved their cognitive function scores according to FAB and MoCA. Scores of anxiety and depression on the Spielberg-Hanin scale also improved significantly. On the FAB scale after therapy, the average scores changed from 12.8±1.3 to 15.9±0.4 points (p =0.04). The average value of cognitive function on the MoCA scale changed from 22.7±0.8 to 24.1±0.7, the indicators were significantly (p =0.02) better than the indicators before treatment. The average score for personal anxiety and depression after treatment was 37.1 ± 0.8 (p = 0.02), which indicates the statistical significance of the results obtained. Situational anxiety also decreased and amounted to 36.2±1.1 points on average (p =0.02). If before the start of therapy the levels of neurotrophic factors were reduced, then after treatment with hopantenic acid the content of BDNF and NGF increased. The level of ciliary neurotrophic factor CNTF decreased slightly, its average value was 381.3±0.8 pg /ml, which is not statistically significant (p = 0.2).

In the second subgroup, the average value on the MoCA scale before treatment was 22.7 ± 1.2, after treatment this indicator was 26.7 ± 1.3 (p = 0.02), which indicates a statistically significant improvement in the cognitive sphere in patients of this group. groups (Table 7). The average value on the FAB scale before treatment was 12.1±0.9, after treatment this figure was 16.2±0.9 (p =0.02).

Table 5. Indicators of cognitive status of patients in the main group and control group

Factor/scale	Main group			Control group			R
	MIN	MAX	Average value	MIN	MAX	Average value	
MoCA	22	25	22.6±1.3	26	29	27.4±0.9	0.02
F.A.B.	eleven	14	12.3±0.9	16	18	17.2±1.2	0.04
SA	44	57	52.4±1.2	24	28	26.7±0.8	0.01
PA	43	59	47±1.3	22	29	27.3±0.7	0.03

Table 6. Indicators of neurocognitive status before and after treatment with hopantenic acid

Factor	Before treatment			After treatment			R
	MIN	MAX	Average value	MIN	MAX	Average value	
MoCA	21	24	22.7±0.8	22	28	24.1±0.7	0.11
F.A.B.	eleven	13	12.8±1.3	14	16	15.9±0.4	0.36
SA	46	57	51.8±0.9	28	39	36.2±1.1	0.01
PA	47	58	52.6±1.4	29	42	37.1±0.8	0.02

Table 7. Indicators of neurocognitive status before and after treatment with choline alfoscerate

Factor	Before treatment			After treatment			R
	MIN	MAX	Average value	MIN	MAX	Average value	
MoCA	23	25	22.7±1.2	24	29	26.7±1.3	0.02
F.A.B.	eleven	13	12.1±0.9	15	17	16.2±0.9	0.02
SA	45	57	51.9±1.1	39	44	43.1±1.8	0.1
PA	44	59	52.7±0.9	42	48	44.9±1.4	0.314

Neurocognitive functions were also significantly better in the group of patients receiving choline alfoscerate. When comparing the indicators of situational and personal anxiety of patients of both groups after treatment, lower indicators are noted in the group of patients receiving hopantenic acid. Thus, choline alfoscerate showed higher effectiveness in restoring cognitive functions, and hopantenic acid more effectively relieves anxiety in patients with HIV encephalopathy.

4. Conclusions

1. Such specific laboratory indicators as: viral load, Level of CD 4 lymphocytes do not show the severity and clinical manifestations of HIV encephalopathy.
2. Despite the improvement in immune status with the use of highly active antiretroviral therapy, nootropic drugs remain an essential component in the correction of cognitive disorders in patients with HIV encephalopathy.
3. In patients with severe anxiety conditions, the drug of choice for the nootropic drug is hopantenic acid; in cases of deep cognitive impairment, the drug of choice for the nootropic drug is choline alfoscerate, which improves the state of cognitive deficit.

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