

Principles of Therapeutic Strategy for Neurological Syndromes in HIV Patients

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Abstract The study was based on data from 103 patients with HIV infection (54.4% of women and 45.6% of men) dispensary registered, aged from 20 to 45 years old. Neuropsychological studies of patients with HIV infection were carried out using special tests, such as: Wechsler Memory Scale (WMS), 7 subtests, Schulte table, and “Incomplete Outlines of Objects” The efficacy of citicoline (1000 mg / day) when added to basic HIV treatment was studied in 53 patients. The comparison group consisted of 50 HIV patients who did not receive neuroprotective therapy. The efficacy of treatment was assessed according to the CGI clinical scale (the scale of the overall clinical impression - Clinical Global Impression).

Keywords AIDS, Neurological syndrome, Diagnostic, Treatment

NeuroAIDS is a common name for various clinical forms of central nerve system disorders developing in HIV/AIDS [5]. Today it is clear that, HIV infection from the stage of asymptomatic carriers passed to the stage of clinical manifestations and already entered polyclinics and clinics [2]. Experience showed that, nowadays that category of patients concentrates not only in the centers and units of AIDs prevention, but more often applies to neurologists in polyclinics and, due to ineffective therapy, they are hospitalized diagnosed with circulatory encephalopathy, polyneuropathy of unclear genesis, disseminated encephalomyelitis syndrome, insult, progressing myelopathy, focal cerebral lesions, leukoencephalopathy, and other pathologies. [3,5,9]

The data of large analytical reviews dedicated to HIV/AIDs neurological problems let us make a conclusion that nowadays there are no effective treatment means for neurological diseases in cases of that pathology. Combined application of modern antiretroviral medicines can lead to normalization of CSF, and sometimes to partial regress of cognitive impairments; it inhibits progression of the pathology, but does not provide recovery of patients with developed dementia. Lethal outcome occurs in average period of 5-6 months [4,8].

There are trials with inclusion of neurometabolic medicines, which are usually used for the treatment of dementia, particularly antioxidants, glyatilin, and symptomatically applied agents in cases of acute psychic

disorders development (atypical neuroleptic Clozapin) to the complex therapy of patients with HIV [1, 7]. It should be taken into account that these patients have increased sensitivity to psychotropic agents. Traditional neuroleptics can cause development of a stable acipetic rigidity syndrome even with administration of small doses [4,6].

The objective was to study the efficacy of neuroprotective therapy, and particularly citicoline prescription in the complex therapy of the basic neurological syndromes in patients with HIV.

1. Materials and Research Methods

Results of 103 registered HIV patients (54.4% women and 45.6% men) in the age from 20 to 45 years old served the basis for the research.

All patients were divided to three groups: 1st group (n=25) with early preclinical stage of the pathology with absence of indications to start HAART; 2nd group (n=53) with clinical manifestations of HIV infection before development of opportunistic infections at the start of HAART; and the 3rd group (n=25) with opportunistic and other cerebral lesions; sex and age were taken into account in the analysis.

The study did not involve active users of psycho active agents and alcohol, patients with acute somatic, psychiatric, and neurological diseases, patients requiring associate therapy with agents providing significant impact on functional parameters of CNS, and pregnant patients.

Neuropsychological studies in HIV patients were performed with the help of special tests such as Wechsler Memory Scale, (WMS). With the help of 7 subtests we assessed operative memory – logical memory – short-term acoustic memory – visual memory – associative memory. We received equivalent parameter of memory (EPM)

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compatible with IQ. Test of attention stability and workability dynamics Schulte's table evaluates work efficiency – workability degree – psychic stability; “Incomplete outlines of subjects” (A.R. Luria) evaluated visual subject gnosis.

For the correction of revealed neurological syndromes we initiated the study of the efficacy of the prescription of neuroprotective agents, and particularly the prescription of citicoline, in the complex therapy. Taking into account existing notions about pathogenesis of basic pathologies of nerve system data of multiple experimental and a great database of available and current clinical studies it should be noted that, Ceraxone (citicoline) is a neuroprotector with a high level of evidence for the treatment of conditions accompanied by ischemic, traumatic or degenerative lesions of neurons.

We analyzed the data of examination of 103 patients divided to two groups. Efficacy of citicoline (1000 mg/day) added to basic HIV therapy was studied in 53 patients. Comparison group involved 50 patients with HIV who did not receive neuroprotective therapy. Citicoline was prescribed according to the following scheme: initial 10 days intravenous infusion 1000 mg, four solutions, then orally 1000 mg for 20 days.

Efficacy of the therapy was assessed with the help of clinical CGI scale (Clinical Global Impression). Clinical Global Impression Scale (CGI) was created in 1976 in the USA National Institute of Psychic Health for collaborative programs. It consists of 3 subscales reflecting the assessment of condition severity, general degree of its improvement according to 7 scores scale, and efficacy index subscale, which is calculated on the basis of a complex of one of four stages of therapeutic effect (noticeable, moderate, minimal, without alterations) and expression of an agent side-effect (absent, insignificant, significant, leveled-off therapeutic effect).

Statistical analysis of the obtained results was performed with the help of variational statistic methods. Reliability of mean difference was assessed on the basis Student's criterion with 95% confidence interval ($p < 0.05$).

2. Results of the Study

On the basis of performed studies we determined that at the early preclinical HIV stages memory impairments were registered in 64% of the examined patients and involved mostly short-term, auditory, and visual types of memory; attention disorders were expressed by exhaustion (51.2%).

With HIV progression, before the development of opportunistic infections, memory impairments were noted in 78% of the patients and involved logical, visual, and associative memories. Attention disorders were expressed by decrease of work efficiency (22.6%), workability degree (43.3%), and exhaustion (66%).

Clinical observations demonstrate that at the early HIV infection stages the most often observed ones are neurotic reactive conditions and manifestations of asthenic-vegetative

syndrome.

Patients of the 1st group had various neurotic disorders such as increased exhaustibility in 8 (32.0%) of them, absent-mindedness in 5 (20.0%), forgetfulness in 7 (28.0%), bad mood in 13 (52.0%), narrowing of interest range in 6 (24.0%), disorders of sleeping in 11 (44.0%), various phobia in 4 (16.0%), vegetative lability in 15 (60.0%) of the patients (Tab. 1).

Table 1. Symptoms observed in the examined patients at the early stage of the pathology (n=103)

Symptoms	1 st group (n=25)		2 nd group (n=53)		3 rd group (n=25)	
	abs.	%	abs.	%	abs.	%
Increased exhaustibility	8	32.0	19	35.8	12	48.0
Absent-mindedness	5	20.0	15	28.3	9	36.0
Forgetfulness	7	28.0	20	37.7	11	44.0
Bad mood	13	52.0	32	60.4	18	72.0
Narrowing of interests	6	24.0	24	45.3	17	68.0
Disorders of sleeping	11	44.0	31	58.5	19	76.0
Various phobia	4	16.0	14	26.4	10	40.0
Vegetative lability	15	60.0	37	69.8	21	84.0

Expression of neurological symptoms depends on the clinical progress of the disease. Particularly high percents were determined among the patients of the 3rd group, i.e. in those cases when clinical manifestations of HIV were accompanied by opportunistic and other cerebral lesions.

Objective examination of the patients demonstrated disorders of orientation in place, time, and personality in 26.2% (27 patients) - 43.7% (45 patients) cases; there were high integrative dysfunctions such as deterioration of memory and attention in 21.4% (22 patients) cases.

Table 2. WMS values in patients with HIV infection

Groups of patients	Mean EPM	Patients with normal values on the memory scale
1 st group	105±5.4 (100–110)	9 (36%)
2 nd group	95.4±3.4 (91–101)	13 (24.5%)
3 rd group	90.1±2.9* (84–101)	5 (20%)

Note: * - reliability of values compared to the 1st group; $P < 0.05$

Even at the subclinical stage of HIV infection (1st group) psychological tests showed that patients had disorders of memorizing and data reproducing process. Average values of equivalent parameter of memory (EPM) determined on the basis of Wechsler's subtests in that group were below normal ones to one standard deviation and were equal to 105±5.4 (100–110), and that corresponded to the range from slight memory deterioration to the lower normal border.

Normal values of EPM (above 110) were noted only in 36% of the examined patients of the 1st group (tab. 2).

With progression of the pathology there was notable reliable decrease of EPM in the 2nd and 3rd groups ($p < 0.05$); average values of which were equal to 96 ± 3.4 (91–101) in the 2nd group and 90.1 ± 2.9 (84–101) in the 3rd group respectively. Part of the patients with normal values on the memory scale in the 2nd and 3rd groups was equal to 24.5% and 20.0%, respectively.

With progression of the pathology we noted reliably significant decrease of EPM in the 2nd and 3rd groups ($p < 0.05$), the average values were 96 ± 3.4 (91–101) in the 2nd and 90.1 ± 2.9 (84–101), in the 3rd group respectively. Part of the patients with normal values on the memory scale in the 2nd and 3rd groups was equal to 24.5% and 20.0%, respectively.

Thus, with progression of the disease, prevalence of memory disorders in HIV patients increased. Fifty two percents of the patients of the 1st group had a slight

deterioration of memory, 12,0% had a moderate deterioration, and there was no case of expressed deterioration of memory (fig. 1).

At the same time patients of the 2nd group in 32.1% cases had a slight deterioration of memory, in 37,7% moderate and in 5.7% expressed one.

In the 3rd group we noted progression of alterations; expressed deterioration of mnesic functions was revealed in 20% of the examined patients, moderate in 32.0%, and slight one in 28.0%.

Detailed analysis of mean scores on subtests evaluating various types of memory proved a reliable decrease in logical and associative memory within the progression from the 1st group to the 3rd one ($p < 0.05$).

Using profound statistical analysis we received a proof of reliable link between CD4-lymphocytes amount and RNA of HIV patients and expression of deterioration in mnesic processes ($p < 0.05$).

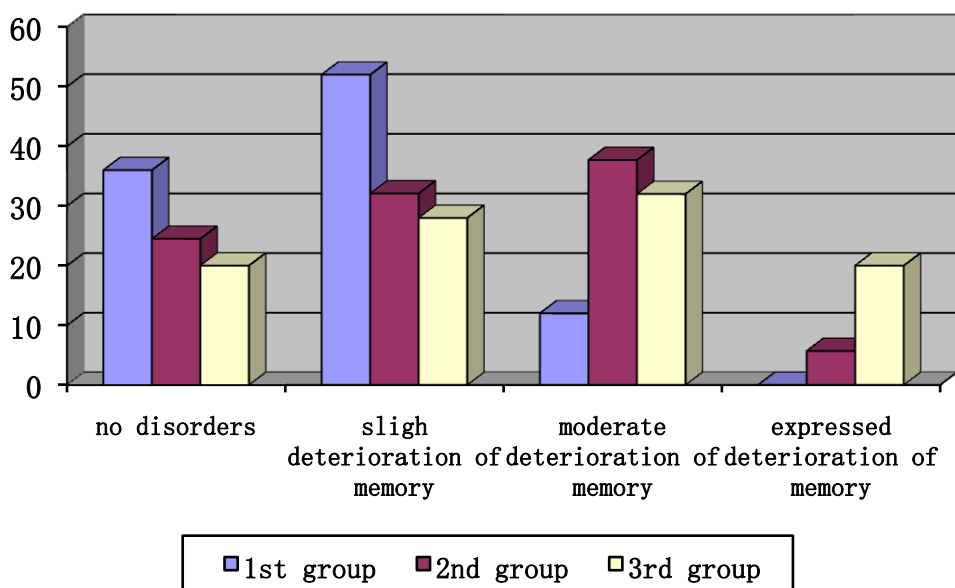


Figure 1. Prevalence of memory disorders in HIV patients

Table 3. Subjective symptoms of HIV patients in the process of therapy (n=103)

Symptoms	Basic group (n=53)				Comparison group (n=50)			
	Prior to therapy		After		Prior to therapy		After	
	abs.	%	abs.	%	abs.	%	abs.	%
Increased exhaustibility	19	35.8	9	17.0*	20	40	17	34^
Absent-mindedness	15	28.3	6	11.3*	14	28	11	22^
Forgetfulness	20	37.7	11	20.8*	18	36	12	24^
Bad mood	32	60.4	11	20.8*	31	62	29	58^
Narrowing of interests range	24	45.3	10	18.9*	23	46	20	40^
Disorders of sleeping	31	58.5	8	15.1*	40	80	35	70^
Various phobia	14	26.4	6	11.3*	14	28	11	22^
Vegetative lability	37	69.8	12	22.6*	36	72	32	64^

Note: * - reliability of data compared to the values prior to the therapy ($P < 0.05$); ^ - reliability of the data compared to the values of the basic group ($P < 0.05$)

In the basic group with the therapy including ceraxone there was no deterioration of patients' condition. None of the patients had side-effects requiring cancelation of the medicine.

In the analysis of subjective symptoms we registered regression of these symptoms; it was expressed among the patients of the basic group; the obtained results are presented in Table 3.

The data demonstrate that the patients of the basic group had almost 2 fold regression of subjective syndromes different from the comparison group ($P < 0.05$).

In the dynamic observation we registered improvement of memory parameters characterized by reliable rise of average EPM values (96.8 ± 2.5 versus 112.6 ± 3.8 ; $P < 0.05$). In the comparison group we also noted a tendency for increase of average EPM. However, there is no reliability, effecting the number of patients with normal values on memory scale. So, while before the therapy deviations were observed in 24.0% cases, after the therapy that part increased by 6.0% ($P > 0.05$), and by 30.2% in the basic group.

As it is seen in the diagram, HIV patients in all groups had a positive dynamics. However, in those patients who received traditional therapy it was less expressed than in the patients with inclusion of citicoline into the complex therapy (fig. 2).

Efficacy of the therapy among the patients of the basic group was 100%, while 46.7% of them had expressed improvement, and 53.3% had moderate improvement of their condition.

Results of the therapy efficacy in the groups of patients, who had traditional treatment, testify longer elimination of subjective and objective symptoms of the pathology. Expressed improvement was noted in 32.0%, and moderate one in 48.0% of the patients.

Twelve percent of patients had minimal improvement of their condition, while 8% had no improvement at all.

Thus, this research demonstrated efficacy of citicoline (ceraxone) prescription in the therapy of neurological impairments in HIV patients.

Detection of early symptoms of manifestation of neurological impairments in HIV cases and in-time prescription of a complex therapy including antiviral agents, vascular medicines, and neuroprotective therapy provides stabilization of patients' condition and decrease of expression and progression of neurological symptoms.

3. Conclusions

1. On the basis of the performed studies it was determined, that at the early preclinical stages of HIV impairments of memory were registered in 64% of the examined individuals and involved mostly short-term auditory and visual types of memory; attention disorders were expressed by exhaustion (51.2%).
2. At the stage of HIV progression up to opportunistic infections impairments of memory were noted in 78% of the patients and involved logical, visual, and associative memories.
3. It was determined that, HIV infected patients, whose complex therapy included citicoline, had double regression of subjective syndromes different from the comparison group ($P < 0.05$) and improvement of memory parameters characterized by reliable rise of average values of EMP (96.8 ± 2.5 versus 112.6 ± 3.8 ; $P < 0.05$).
4. For the purpose of leveling neurological syndromes we proved the efficacy of citicoline inclusion into the complex therapy of HIV patients.

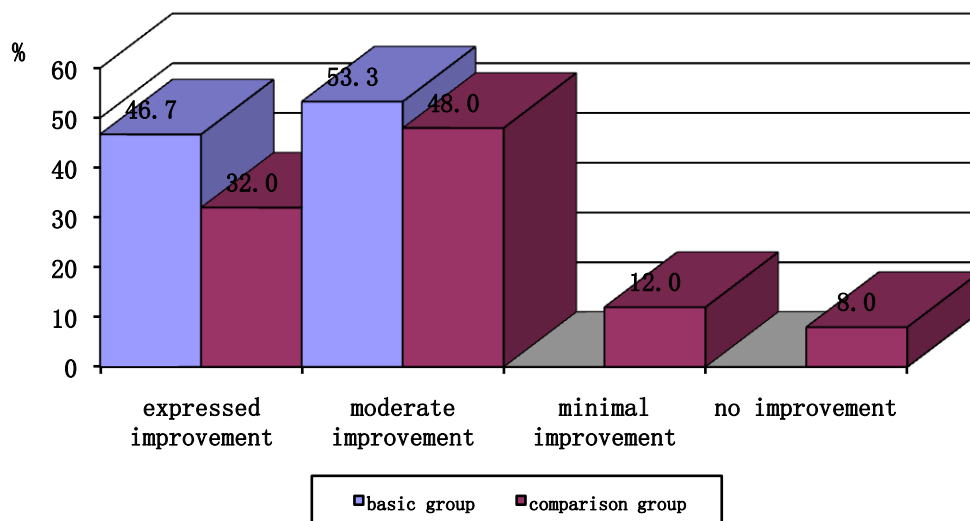


Figure 2. Dynamics of the therapy efficacy according to CGI scale (in 30 days after the therapy)

REFERENCES

- [1] D. Bartlett, D. Galant, P. Fam. Clinical aspects of HIV infection [*Klinicheskiyeaspektivichinfektsii*], M.: R. Valent, 2012. P. 528. (in Russian).
- [2] E.G. Bezrukova. Diagnostic approaches to atypical (neurological) debut of HIV infection [*Diagnosticheskiyepodhodiprinetipichnomnevrologicheskodembyute vichinfektsii*] / E.G. Bezrukova, O.G. Gamov, E.B. Laucart, A.V. Devyatkin, et al // Kremlin Medicine. Clin.bullet. 2014. №4. p.11-17. (in Russian).
- [3] N.A. Belyakov. Comorbid and severe forms of HIV in Russia [*Komorbidniyeityajheliyeformivichinfektsiivrossii*] // HIV and immune suppression. 2016. №3(8). p. 9-25. (in Russian).
- [4] N.G. Zakharova. Causes of unfavorable outcomes in HIV patients administering HAART. Part II. [*Prichinineblagopriyatnihishodovobolnihsvichinfektsiyeprininimavshihvaart*]// HIV and immune suppression. 2015. №4. p.52-63. (in Russian).
- [5] M.F. Ivanova, S.K. Yevtushenko. Early diagnostics of HIV-associated neurological impairments as a topical problem in neurologist practice [*Rannayadiagnostikavichassotsirovannihnevrologicheskikhnarusheniykakaktualnayaprob lemavpraktikenevrologa*] // Intern.neurol.jour. 2016. №8(86). p.53-62. (in Russian).
- [6] Allie S., Stanley A., Bryer A., Meiring M., Combrinck M.I. High levels of von Willebrand factor and low levels of its cleaving protease, ADAMTS13, are associated with stroke in young HIV-infected patients // J. Stroke. - 2015. - N10(8). – P.1294-1296.
- [7] Benjamin L.A. HIV, antiretroviral treatment, hypertension, and stroke in Malawian adults: A case-control // Neurology. – 2016. - N86(4). – P.324-333.
- [8] Cognitive Performance in Men and Women Infected with HIV-1 Jose Maria Failde Garrido, Maria Lameiras Fernandez, Marika Foltz, Yolanda Rodriguez Castro, and Maria Victoria Carrera Fernandez Hindawi Publishing Corporation Psychiatry Journal Volume 2013, Article ID 382126, 6 pages.
- [9] Samantha Simioni et al. Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. AIDS 2010, 24:1243–1250.
- [10] Simioni S, Cavassini M, Annoni JM, Rimbault Abraham A, Bourquin I, Schiffer V, et al. Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. Aids In 2009.
- [11] Stefaniak J. HIV/AIDS presenting with stroke-like features caused by cerebral Nocardia abscesses: a case report // BMC Neurol. – 2015. - N15. – P.183.
- [12] Woods SP, Moore DJ, Weber E, Grant I. Cognitive neuropsychology of HIV-associated neurocognitive disorders. Neuropsychol Rev, 2009; 19: 152-168.
- [13] Yen Y.F., Jen I., Chen M., Chuang P.H., Liu Y.L., Sharp G.B., Chen Y.M. Association of Cytomegalovirus End-Organ Disease with Stroke in People Living with HIV/AIDS: A Nationwide Population-Based Cohort Study// J. PLoS One. - 2016. - N11(3). – P.684.